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Radiological Imaging and Intervention in Venous Thrombosis

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1. Introduction

Radiological imaging plays a central role in the diagnosis, and treatment, of deep venous thrombosis (DVT) in the upper and lower limb. The intention of this chapter is not to distract the reader with a detailed account of the physics behind generating ultrasound (US), computed tomography (CT) and MR (magnetic resonance) vascular imaging. This would demand a chapter in its own right, and this information can be readily found in textbooks. Instead, emphasis will be placed on the clinical indications for requesting imaging in the diagnosis of DVT, as well as the potential limitations of these modalities. This will be supplemented with a review of current evidence and guidelines, and examples of the common image findings. The latest advances in venous MR imaging will be discussed, as will the role of interventional radiology in the treatment of DVT. Finally, considering that it is now universally accepted that DVT and pulmonary embolus (PE) are essentially manifestations of the same disease – namely, venous thromboembolism (Moser et al., 1994) – the imaging and radiological management of PE will also be addressed.

2. Diagnostic imaging in venous thrombosis

2.1 Historical venography

Conventional venography (angiography) has traditionally been regarded as the "reference standard" for imaging the venous system (de Valois et al., 1990). This was performed by opacifying veins with iodinated contrast injected into the vessel via direct puncture, or targeted catheterisation usually from a punctured femoral vein at the groin (fig. 1). Venous imaging has always been challenging with angiography, in particular with the diagnosis of deep vein thrombosis (DVT). Completely occluded veins do not opacify and hence thrombosis has to be inferred rather than directly visualised. Unfortunately, this is compounded by the fact that even normal veins can be rendered invisible by virtue of the direction of venous flow towards the heart, which is counter to the diagnostic need. Contrast injection into an artery will reveal all the distal branches, but the same procedure in veins may not permit adequate visualisation of the tributaries. Furthermore, cannulation of peripheral veins can be hampered by the extent of limb swelling which accompanies DVT.

An additional problem is the small, but recognised, risk of actually causing thrombosis through the irritant effects of iodinated contrast medium on the vascular endothelium.

Even allowing for these limitations, the continued use of conventional angiography is not sustainable in modern clinical practice considering it is a relatively time consuming and hence expensive procedure, and there is a growing demand on hospital Radiology departments to diagnose an increasingly prevalent disorder, affecting 200 per 100,000 of those aged 70- 79 years. The argument for providing a robust and efficient means of diagnosis is augmented by evidence that the initial clinical evaluation of DVT is often ineffective (Barnes et al., 1975; Haeger, 1969, as cited in Fraser & Anderson, 1999). Other conditions including lymphoedema, cellulitis, superficial phlebitis, muscle sprain and ruptured baker's cyst can be indistinguishable from DVT. Indeed, seventy five percent of patients who present with signs and symptoms of DVT do not have the disease (Heijboer et al., 1993; Wells et al., 1995).

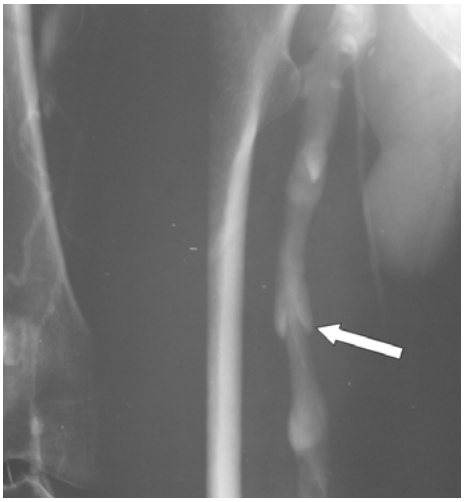


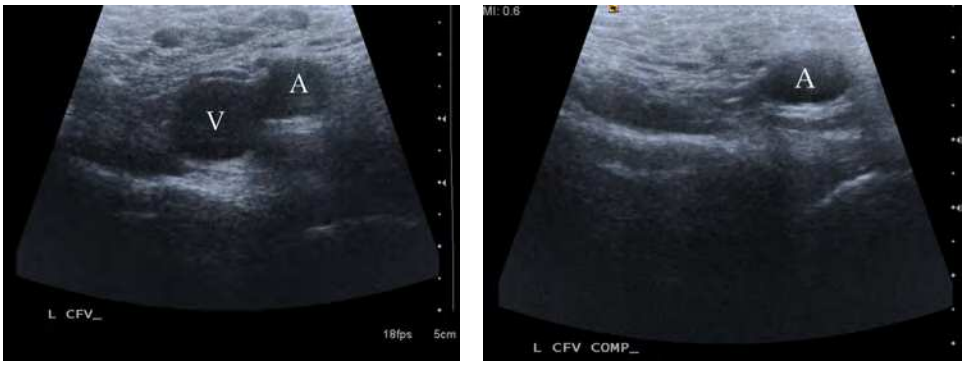
Fig. 1. Lower limb venogram showing a normal superficial femoral vein. Note the normal valves (*arrow*).

2.2 Ultrasound

Ultrasound successfully addresses many of the above requirements, and has clearly become the first line imaging modality in suspected DVT (Cronan, 1993; Dorfman & Cronan, 1992). Unlike other modalities, it can also be a portable technique, allowing assessment of critically ill patients at the bedside. Cronan et al. gathered data from multiple studies to show a sensitivity of 95% and a specificity of 98% in detecting lower limb disease. The performance of venous ultrasound in the upper limb has been less studied, mainly because of the lower incidence of upper limb thrombus. However, the frequency of upper limb venous thrombosis is increasing considering that the two major risk factors are malignancy and central venous catheter placement (Allen et al., 2000; Baron et al., 1998). The performance of upper limb venous sonography should be high as ultrasound provides the highest spatial

resolution of any current imaging modality where veins are sonographically visible (Roditi & Fink, 2009). A relatively large study of upper limb venous sonography including over one hundred patients reported a sensitivity and specificity of 82% (Baarslag et al., 2002).

The most accurate ultrasound tool for diagnosing DVT is compressibility of the vein in the transverse plane; a normally patent vein simply disappears when compressed by the ultrasound transducer (fig. 2). The maximum pressure required to obliterate a vein is much less than that required to deform the adjacent artery. Fortuitously, the entire deep venous system of the lower limb consists of arteries that parallel veins. Compression should not be performed in the longitudinal plane because the transducer may slide off the vessel with compression resulting in a false – positive finding.



(a) (b)

Fig. 2. (a) Transverse ultrasound of a normal left common femoral vein (*V*) and common femoral artery (*A*). (b) Transducer compression obliterates the vein, leaving the accompanying artery unaffected (*A*).

Technique: In suspected lower limb DVT the veins are examined from the inguinal ligament (junction of the great saphenous vein of the superficial system with the common femoral vein of the deep system), to the popliteal vein within the popliteal fossa. There is varying opinion on the usefulness of assessing the distal calf veins, and they are not routinely scanned by the authors in whose institution's protocol employs a repeat interval scan for those with high pre-test probability (see later). There is currently no consensus on what, if any, treatment is indicated in below knee thrombus (Righini, 2007; Schellong, 2007), and the reliability of compression US in excluding calf DVT has been questioned (Dauzat et al., 1997, as cited in Johnson et al., 2010; Kearon et al., 1998). A meta – analysis reported the sensitivity for detecting isolated calf DVT to be 73% (Kearon et al., 1998). Anticoagulation of calf DVT (that might spontaneously resolve) may unnecessarily place patients at increased risk of potential side effects of such medication, with an estimated 1.1% risk of major bleeding (Krakow & Ortel, 2005, as cited in Johnson et al., 2010). This particularly applies to frailer patients vulnerable to intra - cerebral haemorrhage from even innocuous trauma.

Furthermore, the value of adding distal (calf) US to proximal US of the lower limbs for diagnosis of PE was investigated in a sub-analysis of a large, randomised trial. A total of 855 patients with suspected PE underwent investigation by pre – test probability assessment, D-

dimer testing, proximal US and computed tomography pulmonary angiography (CTPA). These patients also underwent distal US, although the findings of this investigation were not used in clinical diagnosis. A total of 59 patients had isolated distal DVT and, of these 59 patients, 21 patients (36%) had no PE on CTPA. Of these 21 patients, 20 patients were not given anticoagulant therapy and had an uneventful follow-up. Thus, in patients with suspected PE, distal US has limited diagnostic value, and a high false positive rate, making it an investigation of limited value for diagnosis of PE (Righini et al., 2008). By contrast, because the vast majority of PEs arise from the pelvis or lower limb, and the treatment for proximal (above knee) DVT is identical to that for proven PE, a positive diagnosis of proximal DVT can eliminate the need to perform imaging of the pulmonary arteries. However, in clinical practice, many patients will have a CTPA, especially if they have respiratory symptoms.

Venous compression technique is known as greyscale imaging. This can be augmented by performing colour Doppler - collectively known as duplex scanning. The Doppler effect is used to analyse blood flow by detecting the change in frequency of ultrasound waves that occurs when sound interacts with moving red blood cells. In the absence of DVT, variations in the Doppler waveform can be elicited by performing simple techniques. By squeezing the calf gently, known as augmentation, the Doppler flow within the venous system proximally increases as the muscle pump drives more blood towards the heart. This helps the operator to confidently exclude clot between the calf and the vein being visualised by the transducer. Another method is to ask the patient to take a deep breath. The increased intra – abdominal pressure during deep inspiration has a compressive effect upon the normal inferior vena cava and pelvic veins, causing a noticeable reduction in Doppler flow, thereby helping to excluded DVT within these proximal veins (fig. 3).

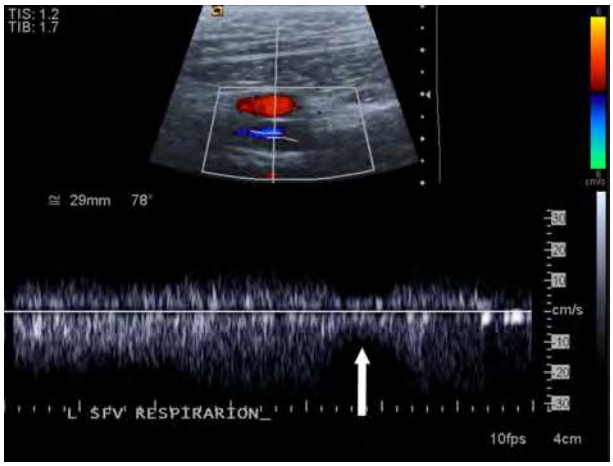
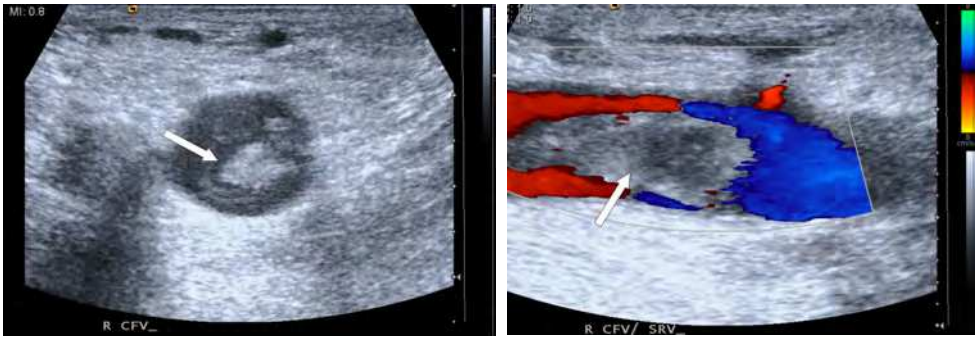


Fig. 3. Duplex US. Normal phasic variation in Doppler waveform within the superficial femoral vein during deep respiration (*arrow*).

Other indicators of thrombus include distension of the vein in acute thrombosis (typically long established clot does not expand the lumen), and visualising clot within the affected vein (fig. 4). Unfortunately, a significant number of acute clots are isoechoic i.e. of the same

ultrasound density to flowing blood, rendering them invisible to the naked eye unless colour mapping is used. Differentiating acute from chronic DVT is a challenge with all imaging modalities, not just ultrasound. The maturation of thrombus from anechoic i.e. less dense than blood, through to hyperechoic i.e. more dense is very variable, and exact age determination is not possible. Six months following a DVT, 50% of patients will have persisting abnormality on US (Dougherty RS & Brant WE, 2007), making the distinction between acute–on–chronic versus chronic changes very difficult. In addition to thrombus appearance, studies have assessed change in thrombus diameter (Kearon et al., 1998), change in thrombus length (Linkins et al., 2004), and Doppler analysis of flow (Prandoni et al., 2002) in an attempt to differentiate acute from chronic changes, but there remains no consensus on which ultrasound measurement can be relied upon to solve this potentially important dilemma. A sensible approach is to obtain a baseline scan at the time of discontinuing anticoagulation to allow for comparison in the event of the patient re–presenting with recurring symptoms.



(a) (b)

Fig. 4. (a) Transverse image showing non – compressible DVT within the right common femoral vein on US. The lumen of the vein contains echogenic clot implying that it is relatively chronic (*arrow*). (b) Longitudinal Duplex image highlighting non – occlusive clot within the common femoral vein (*arrow*) with blood flowing around the thrombus.

Venous Thrombi are dynamic structures, especially within the first 1 to 2 weeks after their onset (O'shaughnessy & Fitzgerald, 2000a, 2000b). Up to 25% of calf DVTs may propagate into the proximal veins (Johnson et al., 2010). Therefore, it is routine practice to repeat a negative scan after 5 to 7 days to assess for propagation into the proximal vasculature, particularly in patients with high pre–test probability scores.

Importantly there are of course limitations to US. As discussed, the calf veins are not readily identified, especially in the swollen oedematous leg, often necessitating a repeat examination to exclude proximal clot propagation. In addition the iliac veins are not readily assessable, and the adductor canal (at the junction of the superficial femoral vein [SFV] and popliteal vein) is notoriously difficult to visualise even in thin patients. The saphenous vein or collaterals can be mistaken for the SFV. In addition, the SFV is duplicated in approximately 20% of patients, potentially leading to diagnostic error, particularly if one system is occluded and the other patent. Obesity and oedema can render examinations

inconclusive. Interestingly, studies have shown that whilst US is sensitive and specific for symptomatic lower limb DVT, it has rather poor sensitivity for asymptomatic DVT compared to conventional venography, with sensitivity between 29 and 38% (Davidson et al., 1992; Turkstra et al., 1997, as cited in Roditi & Fink, 2009). US has been investigated as a potential screening test in asymptomatic patients deemed to be at high risk of DVT following surgical procedures. However, the sensitivity and specificity appear to be reduced in this setting, a randomised – controlled trial discovering no added benefit of screening patients for DVT after lower limb arthroplasty surgery (Robinson et al., 1997, as cited in Fraser & Anderson, 1999).

A final potential pit – fall is worth clarifying, especially for the referring clinician acting upon the radiological report. The superficial femoral vein is actually part of the deep venous system, and thrombus involving this vein could easily be interpreted as only a superficial phlebitis by the unaware clinician. The term should either be avoided, and replaced with the deep femoral vein (the practice of the authors), or the conclusion of the report should clearly indicate that there is DVT.

2.3 Computed tomography and pulmonary embolus

A study performed in 1994 showed that among patients with proximal DVT, approximately 40% had an associated asymptomatic PE, supporting the belief that PE and DVT are essentially manifestations of the same disease, sharing similar risk factors (Moser et al., 1994). Although PE can result from several embolic sources including air, fat, amniotic fluid and tumour, it has been estimated that PE originates from lower limb DVT in at least 90% of cases (Sevitt & Gallagher, 1961). Another common feature of these conditions is their rather non-specific presentation, with clinical signs often being of limited value in confirming a diagnosis (British Thoracic Society, 2003). Only a minority of patients presenting to the emergency department with classic pleuritic chest pain will have PE. Imaging again plays an essential role in diagnosis.

Chest radiography will be the first radiological examination obtained in almost all patients presenting with PE, but a definitive diagnosis cannot be made on chest radiography alone. The majority of patients will have non-specific abnormalities such as airspace opacification, diaphragmatic elevation, linear atelectasis, and possibly cardiac silhouette changes. Conversely, a completely normal chest radiograph can be seen in up to 40%. The principal role of the plain chest radiograph is therefore to detect conditions that can mimic PE, such as pneumonia or pneumothorax.

CTPA is now established as the first line investigation for the diagnosis of PE, surpassing ventilation/perfusion (V/Q) scans, most noticeably by reducing the number of indeterminate, non-diagnostic examinations (Johnson MS, 2002). In addition, CTPA has a superior inter – observer correlation (Blachere et al., 2000), with sensitivities of 94 – 96% and specificities of 94 – 100% being reported (Blachere et al., 2000; Remy-Jardin et al., 2000). Following targeted contrast opacification of the pulmonary arterial tree, multidetector CT allows evaluation of pulmonary vessels down to sixth order branches with the ability to reformat the original data in multiple planes to enhance the diagnostic accuracy (fig. 5). Emboli are recognised as intraluminal filling defects that partially or completely occlude the vessel. The most specific sign of acute PE is a filling defect that forms acute angles to the

vessel wall. Clot forming an obtuse angle implies chronic thromboembolic disease, but this can also be seen in the acute setting. Secondary signs on CT reflect the non-specific abnormalities frequently seen on chest radiography. Pleural based wedge shaped consolidation indicates peripheral haemorrhage or infarction. Peripheral oligaemia (paucity of blood vessels distal to the occluded artery), pleural effusions and linear atelectasis (partial collapse) can also be observed.

Detailed depiction of the lung parenchyma offers additional information not provided by V/Q scans (fig. 6b). In the context of a negative test for PE, an alternative explanation for the patient's symptoms may be highlighted. A study found that as many as two – thirds of patients with an initial suspicion of PE received another diagnosis following CTPA (Hull et al., 1994, as cited in Schoepf & Costello, 2004). In another study, CTPA identified pleural or parenchymal abnormalities that explained indeterminate defects on V/Q scans in 57% of patients (van Rossum et al., 1996, as cited in Kanne et al., 2004). Although a normal V/Q scan essentially excludes PE, a high probability scan has a sensitivity of 88%, compared to 94 – 96% for CTPA (Kanne et al., 2004). Patients with intermediate or indeterminate probability scans (because of background lung or pleural abnormalities) still have a 30 – 40% incidence of PE (Klein JS, 2007). V/Q scans, however, should always be considered in young patients with low pre-test probability and normal chest radiographs in view of its lower radiation dose.

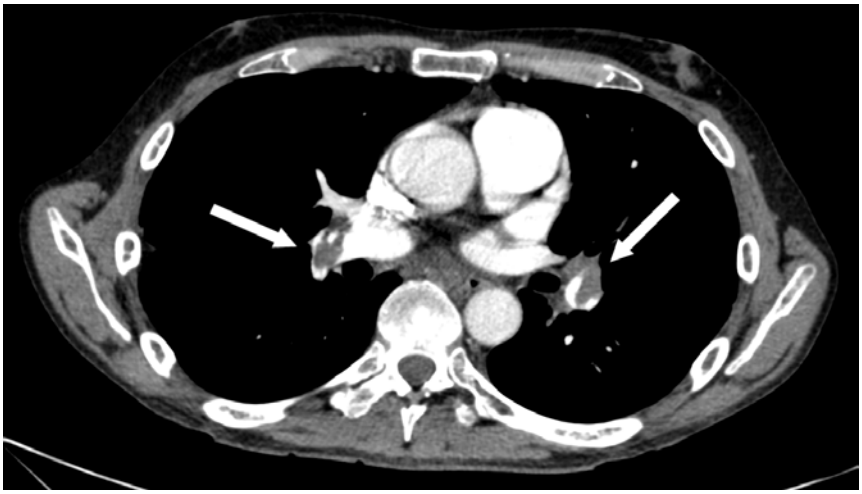
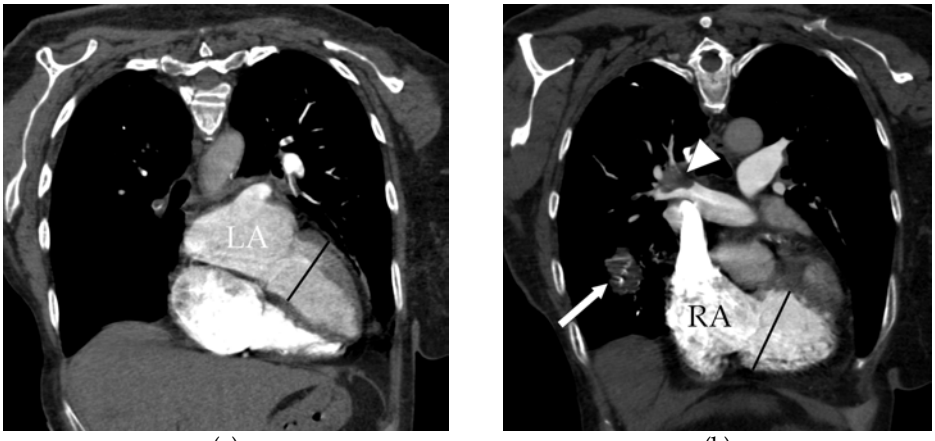


Fig. 5. CTPA in the axial (transverse) plane demonstrating bilateral filling defects within the contrast opacified pulmonary arteries diagnostic of PE (*arrows*).

The main cause of death within the first 30 days after a PE is right ventricular failure (Schoepf et al., 2004). Right ventricular enlargement on CTPA has been shown to correlate with right ventricular dysfunction on echocardiography, and to predict early death from acute PE. In patients with confirmed PE, evidence of right heart strain / dysfunction should always be sought as this can influence patient management with regards reperfusion therapy. To accurately, and reproducibly, measure ventricular size the original CT data is manipulated to allow reformatting in the 4 chamber orientation. This is simply performed at the reporting workstation. The ventricle is measured at its maximum size at a level 1 cm

ahead of the corresponding atrioventricular valve. A right ventricle : left ventricle ratio of > 0.9 is indicative of right ventricular enlargement (fig 6).

CT venography (CTV) can be combined with CTPA to evaluate both PE and DVT in a single CT study (fig. 7). The lower limb veins are scanned at intervals 3 or 4 minutes following completion of the pulmonary angiogram. The sensitivity and specificity of CTV has been reported between 89 – 100% and 94 – 100% respectively (Begemann et al., 2003; Loud et al., 2001, as sited in Kanne et al., 2004). The combined study also allows evaluation of the iliac system, not afforded by US. However, a major concern is the additional radiation exposure. A study found the addition of CTV to increase the gonadal dose by a factor of 500 in women and 2000 in men (the dose is higher in men since the testes are external to the body cavity). This translates to increased likelihood of birth defects and radiation – related death, albeit at a very low added risk (Rademaker et al., 2001). Combined CTV also requires substantial contrast medium dose for adequate venous opacification, significantly greater amounts than the relatively small quantities (50 - 75 ml) required for CTPA on modern multidetector scanners. The value of this combined study is therefore debatable, and CTV is not included in the CTPA protocol in most European institutions, including our own.



(a) (b)

Fig. 6. Coronal oblique reformatted CTPA at the level of the atrioventricular valves demonstrating right ventricular enlargement. (a) Maximum size of the left ventricle (*line*). LA = left atrium. (b) Maximum size of the right ventricle (*line*). RA = right atrium. The corresponding right ventricle : left ventricle ratio is > 0.9. Note the clot within the right pulmonary artery (*arrowhead*); and a lung tumour (*arrow*) which was not clinically suspected.

The value of adding lower limb US in the evaluation of patients undergoing CTPA has been evaluated in a large, randomised trial of 1819 patients with clinically suspected PE. Following pre – test probability assessment, 909 patients were randomised to investigation by D-dimer measurement and CTPA, and 916 patients were randomised to D-dimer measurement, CTPA and venous US of the leg. The primary outcome was 3 month thromboembolic risk in patients who were left untreated on the basis of exclusion of PE by the investigation strategy. The prevalence of PE and the 3 month risk of thromboembolism

was the same in both investigation groups. Thus, venous US of the leg does not improve diagnosis of 3 month thromboembolic risk when added to investigation by D-dimer analysis and CTPA (Righini et al., 2008). Therefore, it can be argued that for patients who have undergone CTPA for the investigation of PE, US of the leg is a redundant investigation.

The diagnostic power of current CT has provoked another interesting debate with the ability to potentially identify clot down to sixth order branches with multi – detector row scanners (MDCT). Older single detector row scanners (SDCT) have limited ability in detecting isolated subsegmental PE. Whilst the treatment of embolus detected within third and even fourth order subsegmental arteries is undisputed, the clinical relevance of detecting clot within smaller, more peripheral branches is questionable (Kanne et al., 2004), and could be unnecessarily subjecting patients to the side effects of anticoagulation. A review of 20 prospective cohort studies and 2 randomised controlled trials was done to evaluate the importance of single and multiple detector row CTPA in the diagnosis of subsegmental PE. This meta-analysis showed that the diagnosis rate of sub-segmental PE was 4.7% with SDCT and 9.4% with MDCT. However, the 3 month risk of thromboembolic events in patients with suspected PE who were left untreated based upon a diagnostic algorithm that included a negative CTPA was 0.9% for SDCT and 1.1% for MDCT. Therefore, although MDCT increases the proportion of patients diagnosed with PE compared with SDCT, it does not substantially reduce the 3-month risk of thromboembolism. The authors suggest that isolated sub-segmental PE may not be clinically relevant (Carrier et al., 2006). Small peripheral emboli are believed to form even in healthy individuals (although this has never been substantiated); and it is a function of the lung to prevent these small clots from entering the arterial bed (Tetalman et al., 1973, as cited in Schoepf & Costello, 2004).

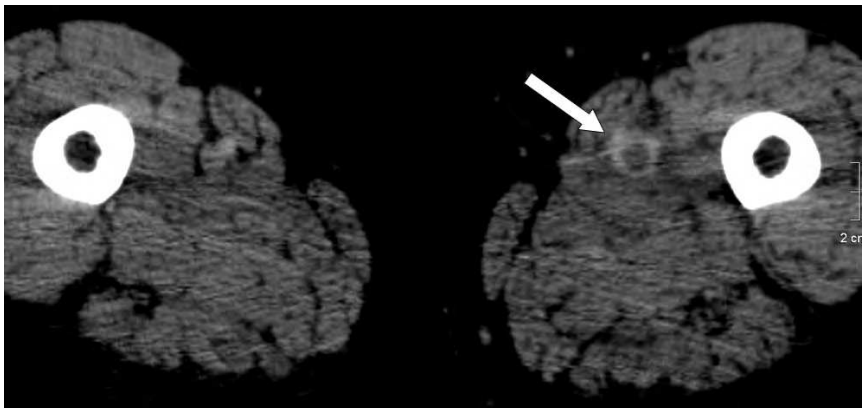


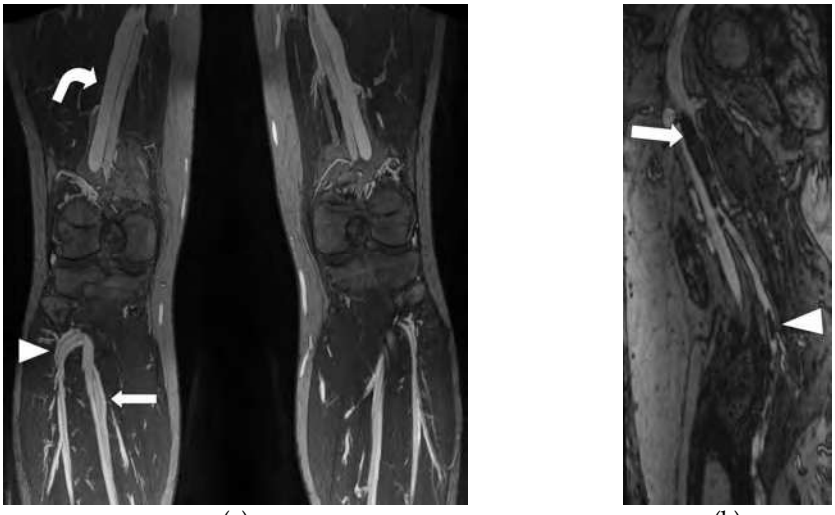
Fig. 7. CTV (combined with CTPA) demonstrating clot within the left superficial femoral vein (*arrow*).

2.4 Magnetic resonance imaging

MRI has been perhaps underutilised in DVT because it is seen as relatively expensive, less accessible and more time consuming compared to other modalities. Furthermore, this probably also relates to the variability of venous enhancement encountered using the wide variety of imaging techniques available (Roditi & Fink, 2009). Despite this, MRI is

undergoing the greatest evolution in terms of venous imaging. Studies have already shown the sensitivity and specificity of MR venography (MRV) to be comparable to conventional venography in diagnosing femeropopliteal DVT (Cantwell et al., 2006; Fraser et al., 2002, as cited in Cantwell et al., 2006). Conventional venography is poor by comparison in opacifying the pelvic vessels (Cantwell et al., 2006; Spritzer, 2009). To reiterate, US also performs poorly in assessing the iliac vessels. Where MRV has perhaps until now performed less well than venography is in assessing the calf veins (Cantwell et al., 2006). With contrast enhanced MRV this was largely because of difficulties in predicting the arrival of contrast in the more distal veins to optimally time the acquisition of the images. This is confounded by the very short transit time of standard extracellular contrast agents within the vascular bed as they rapidly redistribute into the extracellular fluid space.

Recent advancements in the physical properties of contrast agents have overcome the aforementioned difficulties in imaging the calf vessels. The "blood pool" contrast agent gadofosveset trisodium (Vasovist, Bayer Schering Pharma, Berlin, Germany) binds to plasma albumin extending the blood pool residence time. Not only does this eliminate time constraints in acquiring satisfactory images, but allows very high spatial resolution imaging of both the deep and superficial venous system (fig. 8). As previously mentioned, a potential pitfall of venography and US is the not uncommon occurrence of duplicated veins. A study investigating the effects of these anatomical variants in DVT suggested that DVT was twice as likely to be missed (Liu et al., 1986, as cited in Cantwell et al., 2006). Fig. 9 shows duplication of the SFV readily identified by high resolution MRI.



(a) (b)

Fig. 8. High resolution MRI using "blood pool" contrast allows excellent visualisation of both veins and their accompanying arteries. (a) Coronal plane. The normal anatomy of the calf arteries with their accompanying paired veins is clearly demonstrated with the anterior tibial artery and veins (*arrowhead*) and the peroneal artery and veins (*straight arrow*). The superficial (deep) femoral vein and artery are also shown (*curved arrow*). (b). Sagittal oblique view showing clot within the common femoral vein (*arrow*) and great saphenous vein (*arrowhead*).

The lack of radiation makes MRI a more attractive option than CT, particularly when there are concerns regarding pelvic DVT in younger patients as the reproductive organs are within the scanning field. For this reason, MRI should always be considered in excluding DVT in pregnancy. US is often equivocal especially in the latter stages due to technical difficulties. A further venous complication of pregnancy is ovarian vein thrombosis, or puerperal ovarian vein thrombophlebitis. Presentation is usually on the 2nd or 3rd day postpartum with lower abdominal pain and fever. The major complications are septicaemia and PE, which is reported to occur in up to 25%. MR is considered to be more sensitive than CT or US in making the diagnosis (Kubik-Huch RA et al., 1999, as cited in Spritzer, 2009).

Several studies have evaluated the performance of pulmonary contrast enhanced MRA for the diagnosis of PE. One of the larger studies (Oudkerk et al., 2002, as cited in Roditi & Fink, 2009) assessed MRA in 141 patients with an abnormal perfusion lung scintigraphy and compared the findings with those of pulmonary DSA. Sensitivity was 77%, and the demonstration of emboli in two patients with a normal angiogram resulted in a specificity of 98%. The major advantage of MR is the lack of radiation exposure. A study has shown that the radiation from a single CTPA may cause an additional attributable lifetime risk of cancer of almost 1% in young women (Einstein et al., 2007, as cited in Roditi & Fink, 2009), mainly because breast tissue is relatively radiosensitive. With the introduction of "blood pool" contrast agents a comprehensive examination can be performed for PE and DVT using a single low dose contrast injection, without the associated radiation concerns that hamper CT.

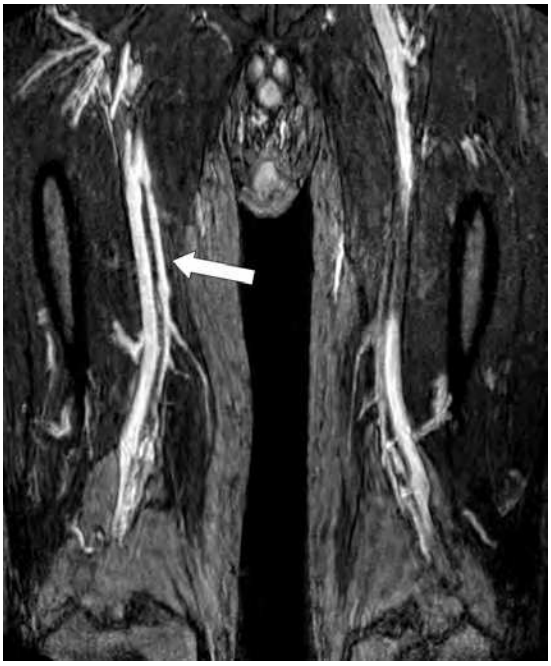


Fig. 9. High resolution MRI in the coronal plane showing duplication of the superficial femoral vein (*arrow*). Note that the superficial femoral artery is not visible because it was occluded at the groin. The patient had known claudication.

The limitations of MR are the relative expense limiting availability, and for some patients the claustrophobic environment preventing completion of the examination. At present, MRI should be considered when there is a strong clinical suspicion of pelvic DVT, and in young women requiring investigation for PE with abnormal chest X – ray precluding a V/Q scan.

3. Role of interventional radiology in venous thrombosis

3.1 Introduction

Despite advances in diagnostic techniques and therapeutic approaches, DVT remains a potentially life threatening disorder. Anticoagulation, which is the current standard of treatment for patients with acutely diagnosed above knee DVT, involves treatment with low molecular weight heparin followed by a 6 month course of warfarin (Hyers et al., 1998). This treatment is designed to stop further progression and potential embolisation, but does not treat or remove the existing thrombus and may be insufficient in treatment of extensive ilio-femoral thrombosis. A large clot burden in the proximal veins in the acute phase can lead to local complications including venous oedema, acute compartment syndrome, tissue necrosis and venous gangrene, and systemic complications such as PE.

Over time normal fibrinolytic mechanisms will result in a variable degree of recanalisation of the thrombosed segment but this may not be sufficient for resolution of clinical symptoms. Chronic DVT and venous insufficiency has been shown to diminish a person`s quality of life and socioeconomic activity (Vedantham et al., 2004).

There are a number of endovascular treatment options in DVT which aim to achieve thrombus removal, restoring patency and potentially limiting the acute complications associated with DVT. It is important to appreciate the limitations of these treatments and the relative lack of randomised controlled trials evaluating the efficacy of these interventions.

3.2 Catheter directed thrombolysis treatment

This technique involves infusion of a thrombolytic agent in and around the thrombus via an infusion catheter. This leads to high dose delivery of the thrombolytic agent locally, reducing the systemic complications, and has been shown to have almost double the venous patency rate at one year, compared to systemic thrombolysis (Comerota et al., 2007). This has been sanctioned by the American College of Chest Physicians (ACCP) as a first line treatment in "selected patients with extensive acute proximal DVT who have a low risk of bleeding" (Kearon et al., 2008). Further criteria include a young patient with a good functional status, life expectancy greater than one year and symptoms for ideally less than 14 days.

Although the administration of the thrombolytic agent is local, the lytic agent can migrate systemically and can increase the risk for major bleeding complications requiring the patient to be monitored aggressively in a high dependency/intensive care setting.

The route for catheter placement is usually decided depending on the thrombus location and burden. This may be placed via the jugular, contralateral femoral or ipsilateral popliteal vein, ideally using ultrasound guided access. Catheters with multiple side - holes and long infusion length can be used for drug delivery and although there is no single drug that has been approved for this use, streptokinase and more recently alteplase (rt-PA) have been

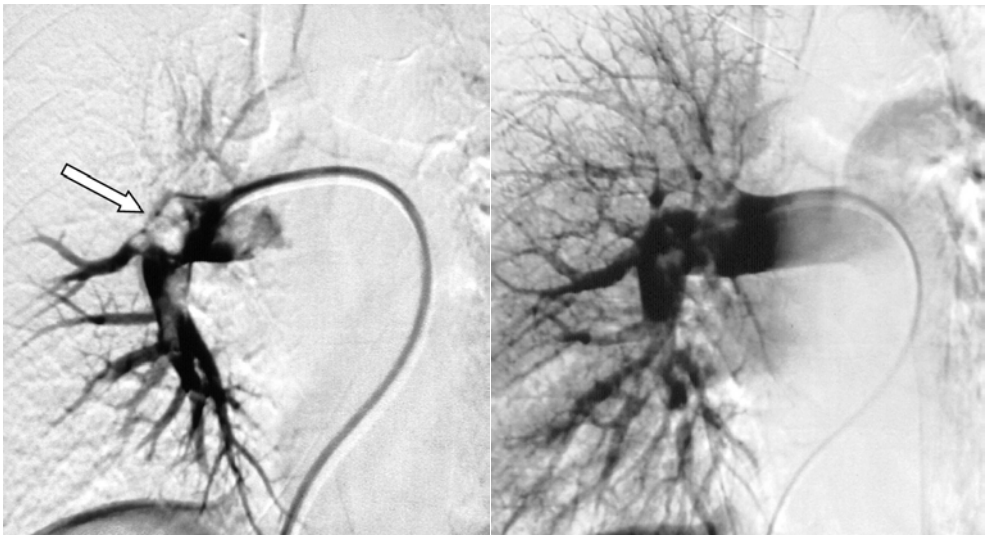
used for this purpose. Venography at the time of the procedure can help assess the clot burden, plan adjunctive treatments (venoplasty, pharmaco-mechanical disruption) and also help define a suitable end point.

There is however a lack of prospective randomised data assessing the benefits of thrombolysis as compared to anticoagulant therapy (Pianta & Thomson, 2011). This, in combination with haemorrhagic complications and lack of awareness among physicians has limited acceptance of this procedure.

3.3 Percutaneous mechanical thrombectomy and pharmacomechanical thrombolysis

This involves use of a mechanical clot removal device such as a Trerotola (Arrow-Trerotola™ PTD®, Arrow, Reading, PA) which is a rotational device or a hydrodynamic device such as Angiojet (AngioJet® Rheolytic Thrombectomy system: Medrad Intervention, Warrendale, PA) . Other devices such as Trellis (Cividien, Santa Clara, California) or the Clot Buster Amplatzer Thrombectomy Device (ATD, Minneapolis, MN) are also available.

The aim is to achieve maceration/disruption of the clot, thus facilitating thrombus aspiration and removal. This is a much less invasive option than open surgical thrombectomy and other advantages include improved clot removal and more rapid restoration of flow. Intensive patient monitoring is also not necessary unlike catheter directed thrombolysis (fig. 10).



(a) (b)

Fig. 10. Catheter thrombectomy. (a) Catheter tip within the right main pulmonary artery, adjacent to embolus (*arrow*). (b) Post – treatment shows disruption of the clot. Note the striking difference in contrast opacification of the pulmonary arterial tree pre – and post – treatment.

Complications include vessel wall and valve injury and kidney failure due to haemolysis. Although patients can experience transient shortness of breath presumably due to pulmonary microemboli, experience gained from thrombectomy of clotted fistulas has shown that concomitant use of a plasminogen activator significantly reduced the risk of symptomatic pulmonary embolism from the procedure (O'Sullivan, 2010).

Pharmacomechanical thrombolysis involves the combined use of a thrombectomy device in combination with catheter directed infusion of a thrombolytic agent. The advantages of this combination include better permeation of the thrombolytic agent and a smaller duration of treatment. Although some devices can lower the systemic dose of the drug, others do not do so.

A retrospective study of 93 patients showed that pharmacomechanical thrombolysis was an effective treatment modality in patients with significant DVT and compared to catheter directed thrombolysis alone, it provided similar treatment success, reduced length of intensive care and hospital stay, and reduced hospital costs (Lin et al., 2006). However, another study has shown that that use of the Trerotola device alone constituted effective treatment of acute ilio-femoral DVT independent of adjunct pharmacological thrombolysis (Lee et al., 2006).

There is, however, a relative lack of randomised data on the use of these devices and further randomised studies are necessary.

3.4 Venoplasty and stenting

Balloon venoplasty is usually performed in patients in combination with catheter directed thrombolysis or pharmacomechanical treatment to help macerate the existing clot or to dilate a venous stenosis which may have been a contributory factor in the development of the DVT. Venous stenosis can occur due a number of aetiologies. Benign causes include May-Thurner syndrome (Ferris et al., 1983), where long standing pulsatile compression of the left common iliac vein by the left common iliac artery leads to development of a venous web. Malignant compression or invasion can be another cause. Chronic deep vein thrombosis can lead to vessel wall fibrosis and development of stenosis.

Unlike arteries, veins have a high elastic recoil and lower rates of flow which leads to less satisfactory results with long term stent patency, in the iliac veins, with a greater than 50% re-stenosis in up to 15% of patients (Hood & Alexander, 2004). These figures are much worse for patients who are hypercoagulable, have longer stent lengths and need infra-inguinal stents.

Stenting an underlying lesion has, however, shown to help prevent or prolong the interval to recurrence and can result in 50% increased patency rate than thrombolysis alone (Hood & Alexander, 2004) and lower recurrence rates of ilio-femoral DVT (up to 73% lower) in patients with May-Thurner syndrome (Oguzkurt et al., 2004). Most experience has been gained with Wallstents (Boston Scientific, Hemel Hempstead, Herts, UK) which are self expanding stents with a good radial strength. Studies have also shown the efficacy and durability of stents in the IVC (Ing et al., 2001; Razavi et al., 2000).

3.5 Inferior vena cava filters

These percutaneously implantable devices are placed in the infra-renal inferior vena cava to reduce the risk of a significant pulmonary embolism (fig. 11). Specific indications include venous thromboembolism with a contraindication to oral anticoagulation or pulmonary embolism despite adequate anticoagulation (Kaufman et al., 2006). There are further uses including patients with DVT who have cancer or burns, and also in high risk trauma and surgical patients. Case selection is paramount and the risks of device implantation and removal must be carefully assessed.

Device implantation is usually via the femoral or the internal jugular vein in a suitable infrarenal position. Cavograms are performed to delineate the renal veins, asses the extent of thrombus and exclude contraindications such as dilated IVC which may not be suitable for standard filter deployment. Suprarenal placement is undertaken if there is thrombus extension into or above the renal veins.

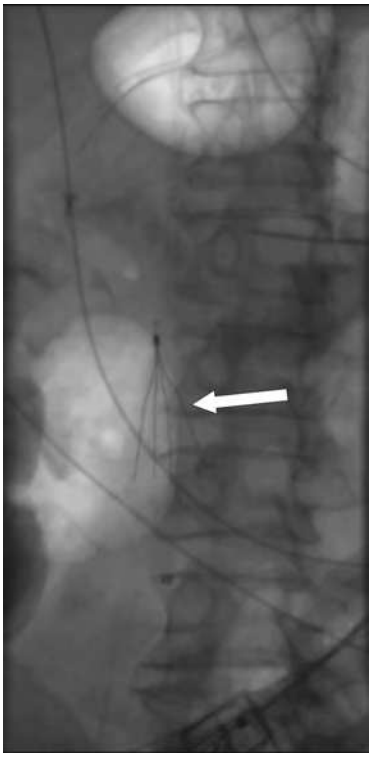


Fig. 11. Temporary IVC filter (*arrow*).

IVC filters are classified as temporary or permanent (Streiff, 2000) and there are various devices available that are approved for use. To cite a few examples, the Bird`s Nest Filter and the Trapease filter are permanent whereas the Gunther Tulip and the Cook Celect Filter are retrievable. Timely removal of retrievable filters is important to reduce the long term

risk of filter deployment. In terms of safety and efficacy, there is no significant difference between the two types of devices (Nazir et al., 2009). Complications associated with the device include those encountered at the time of insertion such as access site haematoma, pneumothorax, inadvertent arterial puncture and misplacement. Delayed complications include IVC thrombosis, occlusion, venous insufficiency and pulmonary embolism.

4. Conclusion

The incidence of deep venous thrombosis is increasing, not just in the lower limb but also within the deep veins of the upper limb, where malignancy and central venous catheter placement are the major precipitating factors. Ultrasound provides a rapid and readily available assessment, and can be portably used at the bedside in critically ill patients. There is however limitations to ultrasound, particularly the poor visualisation of below knee clot. In high risk patients, a short interval repeat scan is indicated to exclude the 25% of such clots which can propagate above the knee.

The iliac veins within the pelvis are also inaccessible to ultrasound in almost every patient. If DVT is strongly suspected within the pelvis, MRI should be considered. This modality has seen the greatest advancements in recent times, with current protocols able to visualise the venous system in very high spatial resolution. CT angiography of the limbs, whilst sensitive and easily incorporated into routine CT pulmonary angiograph in suspected PE, should be avoided in view of the radiation burden. The major advantage of MRI is the lack of radiation exposure. MRI will almost certainly feature more commonly in DVT evaluation in the near future with new "blood pool" contrast agents allowing a comprehensive examination for PE and DVT in the same scan. One specific application is in relatively young patients with abnormal CXR precluding a V/Q scan. However, CT is currently the "gold standard" for diagnosing PE.

There are a number of endovascular treatment options in DVT which aim to achieve thrombus removal, restoring patency and potentially limiting the acute complications associated with DVT. It is important to appreciate there are limitations to these treatments, with a relative lack of randomised controlled trials evaluating their true efficacy. They should however be given consideration in selected patients as outlined above.

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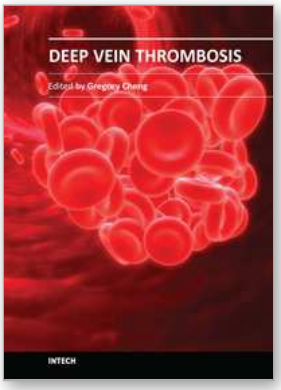

Deep Vein Thrombosis

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This book provides a comprehensive review of deep vein thrombosis. There are chapters on risk factors for DVT, post thrombotic syndrome and its management, vena cava malformation as a new etiological factor and thrombosis in the upper limbs. DVT is usually seen in patients undergoing major surgeries. The guidelines for thrombo-prophylaxis in orthopaedic patients, radical pelvic surgeries, laparoscopic operations and risks versus benefits in regions with a low prevalence of DVT are thoroughly addressed. Cancer and its treatment are recognized risk factors for VTE and extended prophylaxis in ambulatory cancer patients is reviewed. The role of imaging and endovascular therapies in acute DVT, hypercoagulabilty in liver diseases and the challenges in developing countries are discussed.

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