IMAGING OF DEEP VENOUS THROMBOSIS

BJJ Abdullah

We will review the importance early diagnosis of deep venous thrombosis (DVT), the various imaging modalities used and the current imaging protocol used in the diagnosis of DVT in the different groups of patients.

Approximately 80% lower extremity DVT is confined to the calf veins and either lyse spontaneously or organise focally with no further sequelae.[1] However the remaining 20% accounts for 90% of pulmonary emboli. Optimal treatment would require prevention and early diagnosis of DVT since a mortality of 30% has been reported if pulmonary embolism is untreated compared to 8% if properly diagnosed and treated.[2]

There have been numerous different imaging methods used in the diagnosis of deep vein thrombosis (DVT). These include: -

1. VENOGRAPHY

Venography was regarded as the gold standard in the assessment of DVT. There are however several limitations to venography which include the risk of contrast reactions even with the use of non-ionic contrast medium,[3] venous endothelial injury,[4] a 10% rate of inadequate examinations (frequent incomplete filling of the soleal veins),[5] interobserver variations (in about 10 %),[6] as well as the relative increased cost.

2. REAL-TIME ULTRASOUND WITH COMPRESSION AND COLOUR DOPPLER ULTRASOUND (CDUS)

This was initially proposed as an adjunct to the other diagnostic tests but ultrasound (compression and colour Doppler Studies) is now the diagnostic test of choice[7] in the vast majority of symptomatic patients with a suspected diagnosis of DVT. It is also the test of choice in the high risk patients.

Compression of a normal vein would cause the obliteration of the lumen with apposition of the walls and this forms the basis of this study. However in the presence of thrombus the walls would not appose and remain distended. This would allow the diagnosis of thrombus even if the thrombus was ultrasound transparent. A sensitivity of >90% with a specificity of >97% have been quoted in the diagnosis of thrombus in the popliteal and femoral veins.[8-10]

The disadvantage of this technique is the inability to visualise the calf vein consistently. This limitation is of questionable relevance as there are those who would only treat DVT in the popliteal vein or distal to it. The other limitation frequently quoted include the failure to compress the femoral vein in the adductor canal or in those who are obese but this can be overcome by using the hand to support the posterior region of the adductor canal prior to attempting compression.

CDUS allows direct visualisation of lumen of the veins directly which is unlike the use of venography which must show non-filling. It is now the first line imaging technique in the assessment

University of Malaya Medical Center, Kuala Lumpur Malaysia

of venous thrombosis. In the normal vessel the will be complete filling of the lumen with colour. Any consistent absence of colour within the lumen should be considered as being evidence of thrombus. This technique has high sensitivity and specificity (>95% and >98% respectively).[11-13] It can also differentiate between occlusive and non-occlusive thrombus which in a study by Meyerovitz et al[14] showed better recanalisation rates with non-occlusive thrombus. There may also be a role in the follow-up of the rates of recanalisation to compare the different regimes available without the need for additional contrast medium and radiation. It is quick to perform and is cheaper.

It is now possible to demonstrate the flow in normal calf veins with the same sensitivity as above knee studies[15] using CDUS. Only major calf vein thrombus will be detected while small non-occlusive thrombus will not.[11,15] However such small focal clots are unlikely to be of clinical significance requiring anticoagulant therapy. In fact such lesions may also be missed during venography.

What about the iliac veins? They are difficult to visualise with ultrasound. However, iliac vein thrombosis is extremely rare and in addition the femoral veins are invariably involved when there is DVT involving the iliac veins.[16] The patency of the iliac veins and the inferior vena cava can be inferred from the phasic waveform in the external iliac vein as well as a decrease in flow with a Valsalva manoeuvre. The presence of a non-occlusive thrombus may result in the so-called "normal" waveforms. The presence of right heart failure may be another pitfall in using the Doppler waveforms for diagnosis of DVT of iliac veins.

There has been recent work[17] using signal-enhanced colour Doppler sonography in deep venous thrombosis in the lower limbs and pelvis. In this study where echo enhancing contrast medium was injected into the antecubital vein, the number of false positives was reduced from 4 patients to 1 patient while the false negatives was also reduced from 4 patients to 2 patients. The authors suggest that this may have a role in increasing the signal –to-noise ratio of deep veins either in the pelvis or calf veins. This would also reduce the skills required to perform Doppler sonography and make it a more robust technique.

An additional area of uncertainty is that of chronic DVT. Only 50% of DVT's recanalise completely after 6-12 months[18-20] with the rest showing variable degrees of recanalisation and increased echogenicity of the walls. In addition the spontaneous flow is reduced and even absent. Thus in-patients with recurrent symptoms, the demonstration of normal flow except for reduction can be considered normal. However if there are some of the chronic changes, then there is a dilemma since this cannot be reliably differentiated from that of acute DVT.

It must be stressed that even though DVT is mainly confined to the lower limb, the upper limb accounts for approximately 1-2% of DVT. CDUS is an accurate, non-invasive imaging modality with high sensitivity and specificity[21,22] with similar diagnostic criteria. It also may be used to determine the site of subclavian vein prior to central venous line insertion. The limitation however is the decreased sensitivity to subclavian vein stenoses as these tend to lie beneath the clavicle.

3. ^{125}I-LABELLED FIBRINOGEN

This is relatively insensitive to thrombi above the knee joint,[23] which is probably the most important location in deciding the need for treatment. Also the thrombus must be actively propagating for diagnosis.

4. THERMOGRAPHY

Limited by the difficulty in differentiating between superficial phlebitis and other local inflammatory diseases. There is also a wide inconsistent range of sensitivities and specificities (ranging from 33% -97% and 87%-62% respectively).[24,25]

5. IMPEDANCE PLETHYSMOGRAPHY

The limitations of this method are its decreased sensitivity to diagnose non-occlusive thrombus,[26] disease in the calf veins,[27] and to define the specific location of the thrombus which is important to management.

SIGNIFICANCE OF CALF VEIN THROMBOSIS

This is still an area with controversy as regards the clinical management. This stems from two differing schools of thought. Some would argue that thrombus in this area has no risk in propagating proximally[28] unlike others who have shown proximal propagation in up to 20%[29] and therefore require anticoagulants. However DVT predisposes patients to development of the post-phlebitic/post-thrombotic syndrome in 40%-75% of patients.[30] This syndrome can cause significant disabling pain, leg swelling and skin ulceration all of which can clinically simulate recurrent DVT.

Even though rare, over-vigorous compression of the calf veins may result in pulmonary thrombo-embolism[31] and therefore this should be avoided in the obvious cases.

IMAGING PROTOCOL FOR DIAGNOSIS OF DVT IN THE

I. SYMPTOMATIC PATIENT.

Most centres use ultrasound (compression and colour Doppler) as the first line in the management of DVT in the lower limbs. This allows for the assessment of the femoral and popliteal veins

As regards the calf veins, for those that belief that thrombus in the calf veins may show proximal propagation, the calf veins will be examined using compression US with CDUS has proved sensitive and specific provided that the examination was technically adequate. However if the examination is inadequate either a repeat US or venography can be performed. Most centres then confine the examination to only the posterior tibial and common peroneal veins since the anterior tibial veins are regarded as being relatively unimportant.[32] This is because these vessels very rarely contain thrombus without involvement of the other calf veins.[11]

For those centres that do not have the expertise to perform the examination of the calf veins or who belief the calf veins are not associated with thrombus, an initial negative examination is followed by a repeat examination after 48 hours if the patient is still symptomatic. This is to exclude proximal propagation which would normally have done so in that 48 hours. This approach has been justified using outcome analysis.[33] This may not be always feasible since some centres would like to start the treatment as soon as possible.

Thus, some centres resort to venography to solve this problem. In the ultrasound positive cases of DVT in the femoral or popliteal veins, the investigations stop. However in those who have negative study a venogram is done to visualise the calf veins.

Recent evidence shows the only the symptomatic leg should be evaluated[34] since the contra-lateral leg never contains thrombus

immaterial of the presence or absence of thrombus in the ipsilateral symptomatic leg.

II. ASYMPTOMATIC HIGH RISK PATIENT

The imaging protocol in this group of patients (includes those who are at high risk of developing DVT of the lower extremities e.g. patients following hip or knee surgery, previous DVT, etc.) is controversial. The major reason is the thrombi seen in these patients are small and non-occlusive and occurs in the distal vessels of the calf. Colour Doppler techniques thus have problems in detecting the thrombi and result in a high false negative rate with sensitivities of less than 40%.[35] However others have not found no loss of sensitivity above the knee[36] and that this imaging modality may have a role. The same protocol as used in the symptomatic group of repeat examinations after 48 hours may be again applied.

Venography has been considered to be the gold standard of investigation of DVT but there has been a study[37] which showed that studies considered false positive on CDUS had venograms which were incomplete or shown to have DVT at repeat venography.

The role of imaging in these groups may be reduced by the use of prophylactic administration of high molecular flaxiparine to these high risk patients to reduce the risk of DVT.

III. PATIENT WITH PULMONARY EMBOLISM

Immaterial of whether the pulmonary angiogram is appropriate, it is often avoided because of the perceived risk. Ventilation -perfusion scanning was considered the non -invasive imaging method of detecting pulmonary embolism. These studies may however be non -diagnostic or may result in an indeterminate scan. With the advent of Spiral CT, the diagnostic work -up has been modified. It is now possible to non -invasively demonstrate endoluminal clots in the second to fourth order divisions of the pulmonary arteries.[40] Using pulmonary angiography as the gold standard, Garg et al[42] showed that spiral CT had a sensitivity and specificity of 67% and 100% for patients who had indeterminate ventilation/ perfusion scans. The positive and negative predicative values were 100% and 90% respectively. They even suggested that spiral CT may be useful as a primary screening technique for pulmonary embolism. In addition, spiral CT can be mastered by general radiologists and not only by the expert radiologist.[41]

Compression ultrasound has been used by many clinicians to confirm or exclude DVT because of its benign nature. Studies have shown that based on the ventilation perfusion scans, a high probability scan has an up to 60% incidence of DVT demonstrated on colour Doppler US while the intermediate probability and low probability scans have a 55% and 26% chance of DVT respectively.[37,38] Thus CDUS may therefore have a role to play in the management of these patients especially those with intermediate or low probability ventilation/perfusion scans if spiral CT is not available.

However, angiographically proven PE have been shown to occur in approximately 30% of patients with normal bilateral lower limb venography. Thus compression and CDUS cannot be used to exclude the presence of PE.

In patients with known PE but who will not be able to tolerate any further embolic episodes the insertion of IVC filters is of requested. However this will not be necessary in those patients who do not have any residual thrombi in the pelvis or lower extremity. In fact the source of emboli may have been the upper extremity, spermatic or ovarian veins or where the clot from

the lower extremity has completely embolized. In this situation a compression & CDUS may be quite useful in determining the utility of IVC filter insertion.

REFERENCES

1. Hull RJ, Hirsh J, Carter CJ, et al. Pulmonary angiography, ventilation lung scanning and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. Ann. Intern Med 1983;98:98-989.
2. Alpert JS, Smith R, Carlson F et al. Mortality in patients treated for pulmonary embolism. JAMA 1976;236:1477-1480.
3. Lea Thomas M, Keeling FP, Piaggio RB, Treweeke PS. Contrast agent induced thrombophlebitis following leg phlebography: iopamidol versus meglumine iothalamate. British Journal of Radiology 1984;57:205-207.
4. Albrechtsson U, Olsson CG. Thrombotic side-effects of lower limb phlebography. Lancet 1976;1:723-724.
5. Wheeler HB, Anderson FA. Diagnosis approaches for deep vein thrombosis. Chest 1986;89:407-412.
6. McLachlan MSF, Thomas JG, Taylor DW, Kelly ME, Sackett DL. Observer variation in the interpretation of lower limb venograms. Am J Rad 1979;131:451-453.
7. Redman HC. Deep venous thrombosis: is contrast venography still the diagnostic "gold standard". Radiology 1988;168:22-23.
8. Cronan JJ, Dorfman GS, Scola FH, Schepps B, Alexander J. Deep vein thrombosis: US assessement using vein compression. Radiology 1987;162:191-194.
9. Lensing AWA, Prandobi P, Brandjes D, et al. Detection of deep vein thrombosis by real time B-mode ultrasonography. New England Journal of Medicine 1989;13: 121-126.
10. Aitken AGF, Godden DJ. Real time ultrasound diagnosis of deep vein thrombosis: a comparison with venography. Clinical Radiology 1987;38:309-313.
11. Rose Sc, Zweibel WJ, Nelson BD, et al. Symptomatic lower extremity deep venous thrombosis: accuracy, limitations, and role of color Duplex flow imaging in diagnosis. Radiology 1990;175:639-644.
12. Baxter GM, MacKechnie, Duffy P. Colour Doppler ultrasound in deep venous thrombosis: comparison with venography. Clinical Radiology 1990;42:32-36.
13. Lewis BD, Meredith James E, Welch TJ, Joyce JW, Hallet JW, Weaver AL. Daignosis of acute deep venous thrombosis of the lower extremities: prospective evaluation of color Doppler flow imaging versus venography. Radiology 1994;192:651-655.
14. Meyerovitz MF, Polak JF, Goldhaber SZ. Short-term response to throbolytic therapy in deep venous thrombosis: predivtive value of venographic appearence. Radiology 1992;184:345-348.
15. Baxter GM, Duffy P. Calf vein anatomy and flow: implications for colour Doppler imaging. Clinical Radiology 1992;46:198-201.
16. Rose SC, Swiebel WJ, Miller FJ. Distribution of acute lower extremity deep venous thrombosis insymptomatic and asymptomatic patients; Imaging implications. Journal of Ultrasound in Medicine 1994;13:243-250.

17. Puls R, Hosten N, Johannes SB, et al. Signal-enhanced color Doppler Sonography of deep venous thrombosis in the lower limbs and pelvis. J Ultrasound Medicine 1999;18:185-190
18. Baxter GM, Duffy P, Mackechnie S. Colour Doppler ultrasound of the post-phlebitic limb: sounding a cautionary note. Clinical Radiology 1991;43:301-304.
19. Cronan JJ, Leen V. Recurrent deep venous thrombosis: limitations of US. Radiology 1989;170:739-742.
20. Murphy TP, Cronan JJ. Evolution of deep venous thrombosis: a prospective evaluation with US. Radiology 1990;177: 543-548.
21. Falk RL, Smith DL. Thrombosis of upper extremity thoracic inlet veins: diagnosis with duplex Doppler sonography. American Journal of Roentgenology 1987; 149:677-682.
22. Baxter GM, Kincaid W, Jeffrey RF, Millar GM, Porteous C, Morley P. Comparison of colour Doppler ultrasound with venography in the diagnosis of axillary and subclavian vein thrombosis. British Journal of Radiology 1991;64:777-781.
23. Prescott SM, Tikoff G, Coleman RE et al. ^{131}I labelled fibrinogen in the diagnosis of deep venous thrombosis of the lower extremities. American Journal of Roentgenology 1978;131:451-453.
24. Christensen SW, Wille-Jorgensen P, Kjaer L, et al. 99mTc-plasmin scintimetry and 99mTc-plasmin scintigraphy as screening methods for deep vein thrombosis following major hip surgery. Thrombosis and Haemostasis. 1987;58:831-833.
25. Sandles DA, Martin JF. Liquid crystal thermography as a screening test for deep vein thrombosis. Lancet 1985;I:665-668.
26. Jeffrey PC, Immelman EJ, Beantor SR. Comparison of impedance plethysmography with ascending venography for the diagnosis of deep vein thrombosis. South African Journal of Medicine 1985;67:15-18.
27. Ramchandani P, soulen RL, Fedullo LM, Gaines VD. Deep vein thrombosis: significant limitations of non-invasive tests. Radiology 1985;156:47-49.
28. Moser KM, LeMoine JR. Isekmbolic risk conditioned by location of deep venous thrombosis? Annals of Internal Medicine 1981;94:439-444.
29. Lagerstedt CI, Olsson CG, Fagher BO, Oqvist BW, Albrechtsson U. Need for long term anticoagulant treatment in symptomatic calf vein thrombosis. Lancet 1985; 21:515-518.
30. Lindner dJ, Edwards JM, Phinney et al. Long term haemodynamics and clinical sequalae of lower extremity deep vein thrombosis. J Vasc Surg 1986;4:436-442.
31. Perlin SJ. Pulmonary embolism during compression US of the lower extremity. Radiology 1992; 184: 165-166.
32. Nicolaides AN, Kakkar VV, Field ES, Renney JTG. The origin of deep venous thrombosis: a 'venographic study. British Journal of Medicine 1971;44:653-663.
33. Huisman MV, Buller HR, ten Cate JW, Vreeken J. Serial impedance plethysmography for suspected deep venous thrombosis in out-patients. New England Journal of Medicine 1986;314: 823-828.
34. Sheimman RG, McArdle CR. Bilateral lower extremity US in the patient with unilateral symptoms of deep venous thrombosis: assessment of need. Radiology 1995;194:171-173.

35. Mattos MA, Londrey GL, Leutz DW et al. Color flow duplex scanning for the surveillance and diagnosis of acute deep venous thrombosis. Journal of Vascular Surgery 1992;15:366-376.
36. Cronan JJ, Froehlich JA, Dorfman GS. Image-directed Doppler ultrasound: a screening technique for patients at high risk to develop deep venous thrombosis. Journal of Clinical Ultrasound 1991;19: 133-138.
37. Bradley MJ, Alexander L. The role of venous colour flow Doppler to aid the non-diagnostic lung scintigram for pulmonary embolism. Clinical Radiology 1995;50: 232-234.
38. Remy-Jardin M, Artaud D, Fribourg M, et al. Spiral CT of pulmonary embolism: Diagnostic approach, interpretative pitfalls and current indications. European Radiology 1998;8:1376-1390.
39. Garg K, Welsh CH, Feyerabend, et al. Pulmonary embolism: diagnosis with spiral CT and ventilation-perfusion scanning-correlation with pulmonary angiographic results or clinical outcome. Radiology 1998;208:201-208.
40. van Rossum AB, van Erkel Ar, van Persijn EL, et al. Accuracy of helical CT for acute pulmonary embolism: ROC analysis of observer performance related to clinical experience. European Radiology 1998;8: 1160-1164.
41. Barnes RW, Lee Nix M, Barnes CL et al. Perioperative asymptomatic venous thrombosis: role of duplex scanning versus venogram. Journal of Vascular Surgery 1989;9:251-260.
42. Smith LL, Iber C, Irr S. Pulmonary embolism: Confirmation with venous duplex ultrasound as adjunct to lung scanning. Radiology 1994;191:143-147.