



Diagnostic tests

The diagnosis of recurrent deep venous thrombosis

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Summary

Duplex ultrasound is the preferred investigation for the diagnosis of initial and recurrent deep venous thrombosis. The contralateral leg should be scanned when thrombosis is diagnosed as it is bilateral in 30% of cases. At the completion of anticoagulant therapy a venous duplex scan should be performed to establish a new baseline. Recurrent deep venous thrombosis can subsequently be diagnosed if there is a 5 cm increase in the extent of residual thrombus or an increase in the compressed thrombus diameter of more than 2 mm. If there is any doubt about the presence of a recurrent thrombosis serial ultrasound should be used.

Key words: d-dimer, ultrasound, venography.

(*Aust Prescr* 2007;30:38–40)

Introduction

Deep venous thrombosis (DVT) is a common cause of mortality and morbidity with an annual incidence of about 1/1000. It may be complicated by pulmonary embolism and the post-thrombotic syndrome.

About 30% of patients with a proximal thrombosis (involving the popliteal or more proximal veins) who do not receive anticoagulant therapy will develop symptomatic pulmonary embolism within 30 days. Symptomatic pulmonary embolism is dangerous as 25% of cases are fatal. Post-thrombotic syndrome is characterised by pain and swelling of the affected limb and occurs in 50–60% of patients with symptomatic DVT. Graduated compression stockings relieve the symptoms in many cases. However, about 10% of patients will have symptoms that impair their quality of life in spite of compression stockings and about 4% will develop venous ulcers.

Anticoagulation is highly effective in preventing death from pulmonary embolism in patients with DVT. It is indicated for all proximal DVTs and for most cases of symptomatic distal DVT. Therapy begins with low molecular weight or unfractionated heparin followed by long-term treatment with a vitamin K antagonist such as warfarin.

The problem of recurrence

Anticoagulation is highly effective in preventing recurrent DVT, but is associated with a risk of major bleeding of about 3% per year. It is therefore usual to stop anticoagulation six months after a first episode of DVT. Thereafter, DVT is often a chronic and relapsing condition with recurrences in about 30% of patients within eight years. Recurrent DVT is important as it increases the likelihood of post-thrombotic syndrome and is associated with pulmonary embolism.

Risk factors for recurrence

Several risk factors predict the recurrence of DVT. The most powerful of these is whether or not the first thrombosis was provoked by a transient risk factor such as surgery. The annual recurrence rate is 1–3% in patients whose DVTs were provoked by transient risk factors, compared with 8% in patients whose DVTs were unprovoked. Certain clinical, laboratory and imaging factors are also important predictors of recurrence.

Clinical predictors of recurrence include male gender, increasing age and body mass index, active malignancy and neurological disease with paresis of the extremities. Laboratory abnormalities that predict recurrence include thrombophilias such as antiphospholipid antibodies, deficiency of protein C, S or antithrombin and the Factor V Leiden or prothrombin gene mutations. The commonest of these abnormalities are the Factor V Leiden and prothrombin gene mutations but these have only a very weak influence on recurrence. Extensive residual thrombus on imaging studies is also a risk for recurrence.

At present, indefinite anticoagulation is usually recommended after an otherwise unprovoked first DVT in patients with active malignancy or with certain rare thrombophilias (including the presence of antiphospholipid antibodies, homozygosity for the Factor V Leiden and prothrombin gene mutations and multiple thrombophilias). These conditions have particularly high recurrence rates. Although other patients usually stop after six months, studies of the role of longer-term anticoagulation in other sub-groups are ongoing.

Diagnosis of first DVT

The clinical diagnosis of DVT is inaccurate as other clinical conditions may mimic it. Anticoagulant therapy is potentially dangerous as it causes major bleeding in about 5% of cases

of acute DVT within the first three months and 3% per year thereafter. Objective testing is thus required to establish or refute the diagnosis of DVT before treatment. Anticoagulation should not be commenced for suspected DVT without confirmatory objective testing, except in extreme circumstances.

Imaging

Contrast venography was regarded as the gold standard for the diagnosis of DVT, but requires intravenous contrast media and exposes the patient to ionizing radiation. As duplex ultrasound is readily available, safe and accurate it has essentially replaced venography as the first and definitive diagnostic test. For proximal DVT the sensitivity and specificity of duplex ultrasound are greater than 90%.

Duplex ultrasound is the first-line investigation for the vast majority of patients with suspected DVT.

The diagnostic criterion for DVT is incompressibility of the vein when applying gentle pressure with the overlying ultrasound transducer. Additional findings with DVT include the presence of echogenic material within the vein lumen, incomplete filling of the vein with colour Doppler, and lack of the usual variation of the venous flow with respiration.

Duplex ultrasound is operator dependent. Ideally the scan should be performed by a sonographer accredited by the Australasian Sonographer Accreditation Registry who is supervised by a clinician experienced in reporting vascular ultrasound. A comprehensive duplex ultrasound should examine the veins continuously from the inguinal ligament to the ankle. This is effective for excluding DVT so it is safe to withhold anticoagulation if the scan is negative. A positive result is adequately specific for DVT to indicate anticoagulant therapy.

Duplex ultrasound of the contralateral leg should be performed in all confirmed cases as DVT is bilateral in about 30% of patients. This helps avoid diagnostic confusion at a later stage if symptoms then develop in the other leg.

Computerised tomography and magnetic resonance venography are expensive. They offer no tangible advantage over duplex ultrasound.

Laboratory tests

D-dimer is a thrombus breakdown product that is almost always detected in the blood of patients with DVT. Sensitive d-dimer assays (using whole blood or ELISA methods) have been used to exclude DVT and reduce the need for imaging. Patients who have a low probability of DVT, as assessed by a standardised clinical scoring system such as the Wells score¹ (Table 1), and who also have a negative d-dimer test can safely have anticoagulation withheld. D-dimer is not able to exclude DVT in patients with a high Wells score so those patients require diagnostic imaging.

Perform a comprehensive duplex ultrasound scan when anticoagulation is ceased

There are many causes of a positive d-dimer including infection, malignancy, acute coronary syndromes, recent surgery, pregnancy and severe peripheral artery disease. A positive d-dimer is therefore of no diagnostic value. Overall, about 30% of patients in whom DVT is initially suspected will have it excluded by a low Wells score and negative d-dimer testing. In practice, however, d-dimer testing is often performed inappropriately and without reference to the Wells score. For these reasons and because duplex ultrasound is safe, inexpensive and usually accessible, I favour it over d-dimer as the initial test in all patients with suspected DVT.

Diagnosis of recurrent DVT

Duplex ultrasound is the first-line investigation but the diagnosis of recurrent DVT can be difficult. The diagnostic criteria for

recurrent DVT include incompressibility of a previously normal segment of vein or an increase in the compressed diameter of a segment of vein with previously documented thrombus. Both of these criteria require knowledge of the extent of residual thrombus that is present at

the completion of anticoagulant therapy. It is therefore critical to perform a comprehensive duplex ultrasound scan when anticoagulation is ceased, to establish a new baseline against which further scans can be compared. The extent of residual thrombus should be recorded by reference to anatomical landmarks such as the upper border of the patella and the

Table 1
Wells score for clinical assessment of deep venous thrombosis (DVT)¹

Clinical feature	Score
Active cancer	1
Paralysis, paresis or plaster immobilisation of the lower extremities	1
Bedridden for three days or major surgery, within four weeks	1
Localised tenderness along the deep venous system	1
Entire leg swollen	1
Calf diameter more than 3 cm larger on the symptomatic side	1
Pitting oedema greater on symptomatic side	1
Collateral nonvaricose superficial veins	1
Alternative diagnosis more probable than DVT	-2
Probability of DVT:	
low	0
moderate	1 or 2
high	3 or more

saphenofemoral junction. For example, residual thrombus might be reported to extend from 5 cm below the upper border of the patella to 3 cm below the saphenofemoral junction. The compressed diameter of the vein should also be recorded at a number of points. This detailed information is required to interpret the results of subsequent scans and should be provided in the ultrasound report. A detailed diagram of the extent of residual DVT provides a rapid visual assessment of the required information and is particularly useful for subsequent comparison.

A recent study has questioned the reproducibility of duplex ultrasound examinations and has suggested that a change of thrombus length of more than 9 cm is required to accurately diagnose recurrent DVT.² This observation has not been tested in clinical outcome studies and requires replication. Currently, it is my practice to diagnose a recurrence if there is an increase in the length of thrombus of more than 5 cm in a duplex ultrasound scan performed by an experienced sonographer. An increase in the diameter of the vein by more than 2 mm when compressed by the ultrasound transducer also suggests recurrence. Finally, acute DVT tends to have a less echogenic appearance than chronic thrombus although this observation is subjective and has not been studied in comparative or outcome trials. If there is any doubt as to whether there is recurrent DVT then I perform two more scans over the next two weeks. If there is no change in these, then I withhold anticoagulation and only arrange further investigations if there is a significant clinical change. As duplex ultrasound is safe and inexpensive, I have a low threshold to undertake this surveillance program.

Venography may be difficult to interpret in recurrent DVT. Computerised tomography and magnetic resonance venography have no established role.

A negative d-dimer may be of value in excluding recurrent DVT, but is less well-tested than for a first thrombosis. A positive d-dimer test neither confirms nor refutes the diagnosis of recurrent DVT, but necessitates further imaging investigations.

Additional tests

If the patient was thoroughly investigated at the time of their first deep venous thrombosis, there is no need to repeat all the specialist tests. The need for additional tests is guided by the history, examination and basic investigations. If the platelet count is persistently elevated, a myeloproliferative disorder may need to be excluded. A recurrent thrombosis that occurs during anticoagulation could be related to an undetected malignancy.

Conclusion

Recurrent deep venous thromboses can be difficult to diagnose. Identifying a recurrence is easier if the patient had a duplex ultrasound scan when they completed the anticoagulant therapy for their first thrombosis. Although its accuracy depends on the

skill of the operator, duplex ultrasound is safe and relatively inexpensive. It should be the first-line investigation for recurrent deep venous thrombosis.

References

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Further reading

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 55)

3. Magnetic resonance venography is now the gold standard test for the diagnosis of recurrent deep vein thrombosis.
4. After anticoagulant therapy for deep vein thrombosis is completed, the venous system should be assessed by duplex ultrasound.