Controversies and questions in the management of deep vein thrombosis

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The management of deep vein thrombosis (DVT) has changed significantly over recent years with developments in both diagnostic imaging and therapeutic agents. Twenty years ago a patient diagnosed with a DVT would have been admitted to hospital, kept on bed rest and given a ten-day infusion of heparin. Today the vast majority of patients with a DVT are treated in the community.

Deep vein thrombosis is a common condition with an incidence of approximately 1 in 1 000, but in spite of the fact that several cases of suspected DVT are seen in an average size emergency department every day, there are still many controversial issues relating to treatment. In this review I will outline the modern management of a confirmed DVT and address some of the common questions and controversies relating to treatment.

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Management of the acute event

The standard approach to management is an initial course of heparin followed by secondary prophylaxis with warfarin.[1] The low molecular weight (LMW) heparins have now largely replaced unfractionated heparin as the treatment of choice for the management of DVT. These drugs have high bioavailability which means they can be administered subcutaneously once or twice daily, at a dose based on body weight. Monitoring is not required because of the predictable anticoagulant response. It is normal practice to commence treatment with LMW heparin and warfarin simultaneously on day one. The heparin will have full anticoagulant activity within a few hours but the warfarin takes several days to achieve therapeutic effect. It is recommended that LMW heparin is continued for at least five days and should only be stopped when the warfarin has reached a therapeutic level for a period of at least 24 hours.

Table 1. Acute management of deep vein thrombosis

LMW Heparin	Dose	Duration
Enoxaparin (Clexane)	1mg/kg s/c bd or 1.5mg/kg s/c daily	Start on day one Continue for at least five days. Discontinue when the INR has been >2.0 on two measurements 24 hours apart
Dalteparin (Fragmin)	200iu/kg s/c daily	
Tinzaparin (Innohep)	175iu/kg s/c daily	
Start Warfarin on day one at a dose of 5mg daily. Check the INR on day four.		

Thrombolytic therapy is not used in the routine management of DVT because of the high risk of bleeding, but it should be considered for massive limb threatening thromboses as it can rapidly restore vessel patency.[2]

Management controversies

Which clots need treating?

Proximal vein thrombosis

Proximal vein thrombosis is a serious and potentially lethal condition that clearly requires treatment with anticoagulant therapy. Between 40 and 50% of patients with a proximal DVT have evidence of pulmonary embolus (PE) on lung scan[3] and it has been estimated that the incidence of fatal PE may be as high as 10%. As well as the immediate risk there is also a high recurrence rate at 20% to 50% for inadequately treated proximal DVT.[4,5]

Calf vein thrombosis

The management of calf vein thrombosis remains difficult. The literature is confusing and contains contradictory recommendations. The immediate risk of PE from an untreated calf

vein thrombosis is less than 1%, however the main concern is that these clots have the potential to extend into the proximal vessels, which is reported to occur in up to 20% of cases.[6,7] Therefore unless there is a contraindication to anticoagulants, it is recommended that calf vein thromboses should be treated. In patients with a high risk of bleeding, an alternative is to monitor with serial ultrasound scans to identify clots propagating into the proximal vessels. It is no longer acceptable to leave a calf vein thrombosis without any intervention.

Table 2. Recommended duration of treatment

	Type of DVT	Duration of anticoagulation
Proximal DVT	Spontaneous	At least six months
	Precipitated	Three to six months
Calf DVT	Spontaneous	Three to six months
	Precipitated	Three months
Recurrent DVT		Extended to two years Indefinite after several events
Muscular vein thrombosis		• Nonsteroidal anti-inflammatories for seven days • Rescan if symptoms unchanged or worse • Consider LMW heparin for 10 days

Calf muscle vein thrombosis

Over the last few years the sensitivity of ultrasound scanning has improved considerably and it is now possible to identify thrombi in the small veins within the gastrocnemius and soleus muscles. These muscular vessel thrombi have a low incidence of progression to the deep vessels and probably only require symptomatic treatment with anti-inflammatory agents. However if symptoms do not resolve within about a week a repeat scan should be considered. A short course of low molecular weight heparin may be necessary if symptoms persist.

How long to treat?

After the initial treatment with LMW heparin, oral anticoagulant therapy is continued as secondary prophylaxis to prevent recurrence. The optimum length of treatment has been addressed in at least ten clinical trials. It is now generally agreed that the minimum period of anticoagulant treatment following a DVT is three months. This is for patients with a reversible risk factor, for example postoperatively or following trauma. In this group the rate of recurrence of a further thrombosis is less than 5% during the first year after stopping warfarin. In contrast, patients with an unprovoked DVT have a recurrence rate of at least 10% per year and in one series it was as high as 27%.[8,9,10] Choosing the optimum length of treatment for these cases is difficult. It is well established that patients on long-term warfarin have a lower incidence of recurrent DVT than patients who stop treatment after six months. Therefore if warfarin was without complications, long-term treatment would be beneficial in all cases. However in practice the benefits of warfarin have to be weighed against the risk of bleeding. Overall the rate of fatal bleeding from warfarin is 0.6% per annum and is significantly higher in the elderly. Therefore on risk-benefit analysis, six months is the optimum treatment period for an unprovoked DVT in the elderly, but a longer course of treatment may be appropriate in younger patients.

Common questions

Should a patient with an acute DVT be on bedrest?

There is a fear amongst clinicians that physical activity could dislodge a thrombus and cause a pulmonary embolus. However two studies have shown that the incidence of PE is not affected by early ambulation. In fact activity may be beneficial. In one study the progression of thrombus size was less in the mobile patients than those confined to bed and walking exercises were able to reduce pain and oedema more rapidly.[11]

Do compression stockings have a role in the management of DVT?

There is little evidence that compression stockings have any role in the acute management of DVT, but may have a place in preventing the long term complications of thrombosis. Proximal vein thrombosis can often result in damage to valves within the venous system. This can lead to vessel incompetency with venous hypertension and poor venous return, which in turn can result in post phlebitic syndrome. This condition can range from a minor disorder with slight peripheral oedema to a much more serious chronic problem with painful swelling, skin induration and ultimately ulceration. It is reported to occur in up to 60% of patients with a proximal vein thrombosis. This is a difficult condition to manage but there is some evidence that compression stockings may help to prevent the condition by compressing the superficial veins and improving flow through the deep venous system. One randomised study has demonstrated that below knee compression stockings worn regularly (removed at night) for two years reduced the incidence of post phlebitic syndrome by approximately 50%.[12]

Should a woman with a personal history of DVT take an oral contraceptive or use hormone replacement therapy?

It is more than 30 years since the first reports suggested a link between oral contraceptive use and venous thrombosis. Since then numerous studies have addressed this problem. It is now clear that the oestrogen content of these products has a major influence

on the relative risk of thrombosis. With present low dose combined oral contraceptives the overall risk of thrombosis is in the order of four times normal. For many years it was widely accepted that the progestagen content of the pill had little effect on thrombosis, but concerns about the high incidence of thrombosis in users of the 3rd generation oral contraceptives have raised questions about this assumption. It is now recommended that second generation combined oral contraceptives are used as first line oral contraceptive treatment. Women who have unacceptable side-effects and cannot tolerate these agents could be considered for a 3rd generation pill, but the risks of thrombosis must be explained and the patient should be given the relevant Ministry of Health leaflet.[13]

It is advised that women with a personal history of venous thrombosis should not be given oestrogen-containing oral contraceptives. However if a DVT is diagnosed in a woman on an oral contraceptive, treatment does not need to be discontinued immediately. In fact this is potentially dangerous as it may expose a woman to the risk of pregnancy while taking warfarin. It is more appropriate to continue with an oral contraceptive while the patient is on anticoagulant therapy and arrange to discuss alternative forms of contraception before the anticoagulants are discontinued. A progesterone only pill is probably a safe alternative. A WHO study reported that the risk of venous thrombosis was not significantly increased in women using a progesterone only contraceptive, but the risk of venous thrombosis was increased in women who used higher doses of progesterone for menstrual disorders.[14]

The situation is similar for women using hormone replacement therapy. In three studies HRT has been shown to be associated with an increased risk of venous thrombosis with a relative risk of more than two. Therefore HRT should be avoided in women with a history of thrombosis. Again there is no need to suddenly stop treatment, but withdrawal can be managed in a more controlled manner during the course of anticoagulant therapy.[15,16,17]

For many women changing contraceptive therapy or stopping HRT is a major decision and emphasises the importance of making a correct diagnosis of DVT.

How should I advise a patient about future air travel?

The risk of venous thrombosis associated with air travel has gained major media attention over the last few years following a few high profile cases. As a result it has become widely accepted that the 'economy class syndrome' is a real entity on the basis of virtually no evidence.[18] A number of small studies suggest an association between travel and thrombosis but a large case controlled study is needed to demonstrate a clinically significant link. None the less it theoretically makes sense that a prolonged period of immobility in a cramped position, in a relatively hypoxic environment with some degree of dehydration is likely to be associated with an increased risk of thrombosis. It is therefore not unreasonable to advise patients with a previous history of DVT to take some precautions when flying long distance.

In all cases it is sensible to emphasise the simple measures – these include good hydration, avoiding large amounts of alcohol and simple exercises such as rotating the ankles and contracting the calf muscle. Taking the opportunity to walk around the plane is also sensible but not always easy! Below knee compression stocking should be recommended, although the evidence of a significant benefit is small,[19] they are not associated with a high risk of complications. All additional measures for patients with a personal history of DVT remain controversial. There is no evidence to show that low dose aspirin reduces the incidence of travel associated DVT, but as aspirin is known to have an antiplatelet effect it may have a theoretical benefit. However it should be used cautiously, especially in patients who have not previously taken aspirin and those with any gastrointestinal symptoms. Remember that DVT associated with travel probably occurs less frequently than bleeding from aspirin. It may not be wise to risk gastrointestinal bleed immediately prior to a 20 hour flight. Similarly there is no evidence to support the use of LMW heparin given prior to a flight. However it is sensible to discuss this treatment option with most patients with a recent history of DVT as it is easy to administer and has few side-effects. I would only recommend it in a patient who has previously received LMW heparin but feel it is appropriate in patients with a high risk of recurrent thrombosis. This high risk group includes patients who had an unprovoked DVT (with or without thrombophilia) or have an underlying malignancy. It is also prudent to consider this treatment in anybody with a previous travel-related clot. I

Key Points

- There is no evidence that a patient with a DVT should be confined to bed.
- Correctly fitted below knee compression stockings reduce the incidence of post phlebitic syndrome in patients with a proximal DVT.
- Oestrogen containing drugs are contraindicated in women with a personal history of DVT and should be used cautiously in those with a strong family history of thrombosis.
- Progesterone only oral contraceptives are safe alternatives as these have not been shown to be associated with an increased risk of thrombosis.

recommend a treatment dose prior to a flight of more than five hours.

Screening for thrombophilia

The place of screening for inherited or acquired forms of thrombophilia in patients with a first episode of DVT is not clearly established. It could be argued that screening should only be carried out if the results will alter future management. It should be recognised that the presence of inherited thrombophilia does not affect the management of the acute thrombosis, the duration of anticoagulant therapy, the intensity of anticoagulation or the recurrence rate of thrombosis. The risk of recurrent thrombosis may be higher in patients with two or more inherited types of thrombophilia (e.g. Protein S deficiency and Factor V Leiden) but these cases are rare. Screening for the antiphospholipid syndrome is probably appropriate in all cases as these patients have a high risk of recurrence and may benefit from long-term warfarin.

In practice, thrombophilia screening for inherited disorders is probably appropriate in patients with a first thrombosis before the age of 50 years and in patients with recurrent events. In these cases the presence of an inherited thrombophilia can be helpful in discussing treatment options and for family counselling.

Co-ordinating care

The investigation and management of venous thrombosis is often straightforward, but significant problems can result from misdiagnosis, treatment failure and anticoagulant related bleeding. Although the trend is for more patients with DVT to be managed out of hospital, it should be remembered that venous thrombosis is a potentially life-threatening condition and all complex cases should be under the care of a specialist team. The management of DVT requires close co-operation between general practice, the emergency department, diagnostic services, the inpatient medical unit and district nurses. To facilitate an efficient service, many hospitals in New Zealand have established a dedicated thrombosis unit run by specialist nursing staff. This allows good continuity of care with specialist input at all stages. The key to the success of this type of service is close liaison between medical and nursing staff, which allows patients to be smoothly transferred from inpatient to outpatient care.

Advice about flying

- Maintain good hydration
- Simple exercises
- Below knee compression stockings
- Avoid alcohol
- Low dose aspirin has no proven benefit, but may theoretically reduce the thrombosis risk. Only recommend in patients who have previously tolerated aspirin without problems
- For high-risk patient consider a single dose of low molecular weight heparin

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