

Key points

- Calf vein thrombosis has a low but still significant risk of pulmonary embolism and thrombus extension, and should not be ignored.
- Superficial venous thrombosis is associated with inflammatory symptoms and has the risk of possible extension of the thrombus to involve the deep vein system.
- Duplex ultrasound should be used to assess both calf vein and superficial venous thrombosis.
- Anticoagulation with low molecular weight heparin or fondaparinux is the preferred treatment for calf vein thrombosis and superficial venous thrombosis.
- Active surveillance is an option for patients with calf vein thrombosis who have a high risk of bleeding, a low risk pattern of disease or less severe symptoms.
- Topical anti-inflammatory treatments and surveillance is an option for patients with superficial venous thrombosis who have a high risk of bleeding or a very small localised thrombosis.

Calf vein thrombosis and superficial venous thrombosis

Advice on management

DAVID ROBINSON MA, FRACS

Venous thrombotic problems are common in clinical practice, and management guidelines for DVT and pulmonary embolism are well established. However, the optimal management of calf vein and superficial venous thrombosis is more controversial.

Problems related to venous thrombo-embolism, including deep venous thrombosis (DVT) and pulmonary embolism, are common in clinical practice. The annual incidence of DVT (in the leg, defined as thrombosis involving the popliteal or more proximal deep veins) is 80 cases per 100,000 and a large percentage of these are now diagnosed, assessed and treated in the primary care setting. Treatment guidelines for DVT and pulmonary embolism are clearly established – the goals are to prevent (further) pulmonary embolism and to minimise post-thrombotic syndrome. These are best achieved by the early institution of therapeutic anticoagulation, for a duration depending on the underlying cause of the thrombotic episode and any other associated risk factors.^{1,2}

Venous thrombotic events that do not fall

into the diagnostic categories of DVT (as defined above) or pulmonary embolism are associated with more difficulties in management, and seem to prompt more calls to a vascular surgeon than almost any other problem. Calf vein thrombosis and superficial venous thrombosis in particular can pose difficult problems. Clear guidelines are lacking regarding how best to care for patients presenting with these problems. The aim of this article is to attempt to shed some light on the current evidence and provide advice in terms of management.

This is an exciting time in the management of thrombotic disorders with the recent listing of rivaroxaban on the PBS for the treatment of DVT. It is likely that it will have a useful place in the treatment of calf vein and superficial venous thrombosis, but at present it is not indicated for those conditions and its usage

Dr Robinson is a Vascular Surgeon who is a VMO at Royal Prince Alfred Hospital, Camperdown, and in private practice at the Sydney Adventist Hospital, Wahroonga; Macquarie University Hospital, North Ryde; and the Mater Hospital, Crows Nest, Sydney, NSW.

and utility in that situation is unknown. (Dabigatran and apixaban are not currently indicated for the treatment of DVT, only its prevention, and their place in the treatment of calf vein and superficial venous thrombosis has yet to be elucidated.) Therefore, this article is confined to commenting on the evidence base for the treatment of these conditions.

CALF VEIN THROMBOSIS

Calf vein thrombosis refers to the situation where one or more of the deep veins of the calf demonstrate evidence of thrombosis without involvement of the popliteal or more proximal veins. The calf veins comprise three paired veins, the peroneal (or fibular), anterior tibial and posterior tibial veins, and two nonpaired muscular veins, the gastrocnemial and soleal veins (Figure 1).

Better imaging and the institution of more rigorous scanning protocols mean that more patients are likely to be diagnosed with calf vein thrombosis. The anterior tibial veins are now generally not routinely imaged, several studies having demonstrated that the incidence of solitary anterior tibial vein thrombosis is essentially zero.³

The management of calf vein thrombosis is problematic for several reasons: the natural history is poorly documented, there is a paucity of well-conducted trials to help guide or inform decision-making, and the long-term outcome has not been well studied and is poorly known. In general terms, however, the aims of treatment in patients with calf vein thrombosis are the same as in those with DVT – that is, to prevent extension and/or pulmonary embolism and to minimise the risk of post-thrombotic syndrome.

Extension and embolism

Several studies have shown that patients with calf vein thrombosis may also have pulmonary embolism, although there are clear methodological problems with these studies that make it difficult to establish the site or source of thromboembolism. However, in patients presenting with calf vein thrombosis there is an up to 30% risk of extension of the thrombus, and half of these extensions will be into the

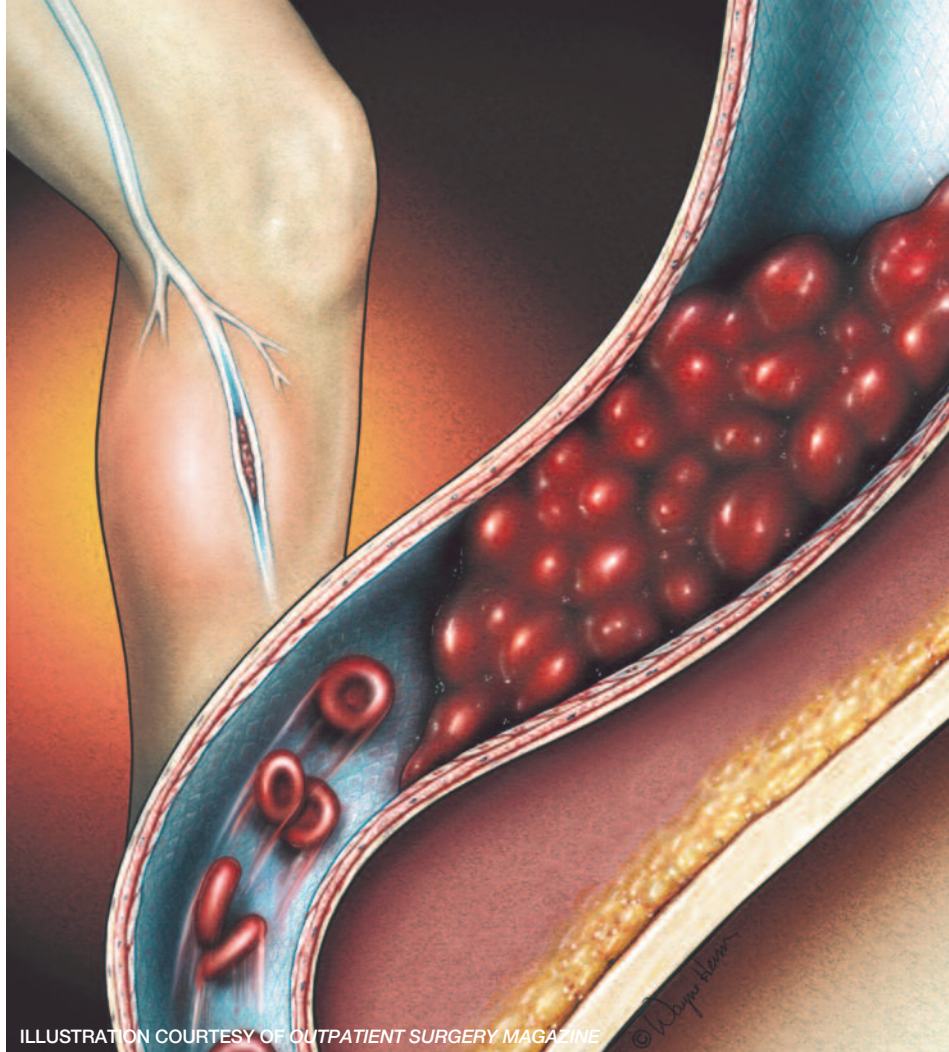


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deep veins (i.e. the popliteal vein or more proximal veins), with attendant risks of pulmonary embolism and post-thrombotic syndrome.

The incidence of pulmonary embolism in patients with calf vein thrombosis who are kept under surveillance varies between zero and 6%. In those patients in whom the calf vein thrombosis involves muscular veins only, the likelihood of extension seems to be lower, with some studies suggesting the risk varies between 3 and 15%. If the thrombus is small (less than 5 cm) or confined to a single calf vein, it seems the risk of extension is lower.⁴

Post-thrombotic syndrome

Post-thrombotic syndrome refers to the constellation of signs and symptoms related to venous insufficiency that may develop after venous thrombosis. The potential for a patient developing this syndrome following an isolated calf vein thrombosis seems to be low, but once again the heterogenous quality of the literature available makes this difficult to determine.

The reported incidence of clinical problems due to post-thrombotic syndrome after calf

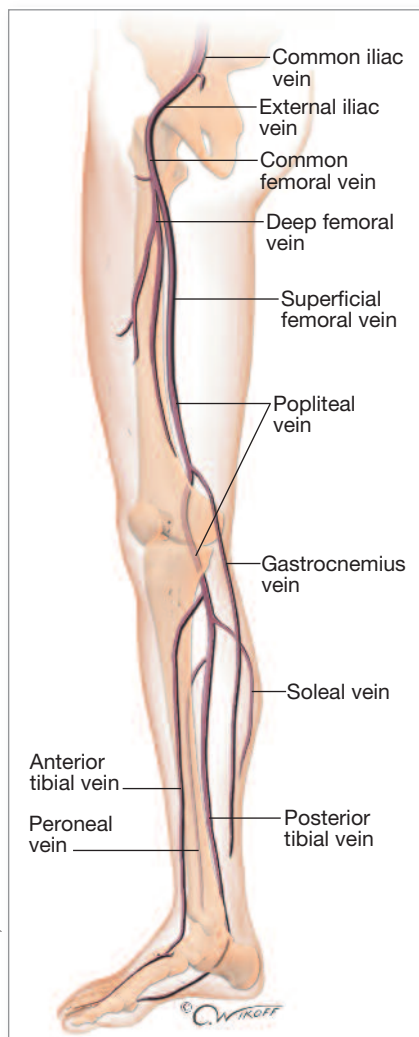


Figure 1. Deep veins of the leg. Note the superficial femoral vein is a deep vein.

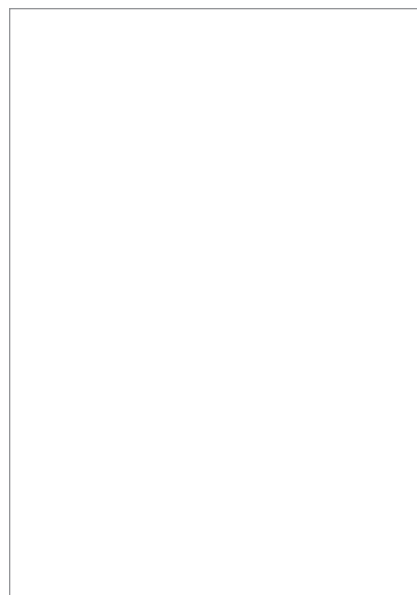
vein thrombosis varies widely, from 10 to 60% according to one review.⁴ Most of these problems will be confined to pain, varicose veins or swelling, with fewer than 5% of affected patients going on to develop problems with varicose eczema or lipodermatosclerosis. As would be expected with a relatively circumscribed problem, ulceration is an unusual event.

Treatment

Calf vein thrombosis has a low but still significant risk of pulmonary embolism

and thrombus extension and, therefore, should not be ignored. Current management consists of either anticoagulation or surveillance.

Surveillance does not mean doing nothing. Surveillance has the benefit of avoiding anticoagulation but means commitment on the patient’s part to a schedule of two or three duplex ultrasound scans a week for several weeks, which represents



a substantial inconvenience to the patient in addition to a significant cost. Current recommendations (anecdotal) are scans for two weeks, but there is good evidence from several studies that thrombus extension or recurrence may occur beyond this time frame.

The American College of Chest Physicians recommendations are for anticoagulation for three months in patients with isolated acute calf vein thrombosis who have severe symptoms or risk factors for extension, which, as they note, is a weak recommendation given the poor quality of the available evidence.² However, six weeks of therapeutic anticoagulation with low molecular weight heparin (LMWH) or fondaparinux is safe with a low incidence of major bleeding, and is generally easy for patients to manage at

home. From a cost–benefit point of view, a local analysis has not been done but US data suggests little difference compared with surveillance.

Given all of these factors, anticoagulation with LMWH or fondaparinux for six weeks is the preferred approach, with active surveillance an option for those patients with a high risk of bleeding or a lower risk pattern of disease (such as a muscular vein thrombosis). In a patient with a clear provoking factor that is not going to persist and who does not want to be anticoagulated, once again active surveillance is a reasonable option.

Natural history of thrombosis

A factor to discuss with patients early in the course of their treatment for calf vein thrombosis (and also with patients with superficial venous thromboembolism) is the natural history of their thrombus. There is a significant tendency for the thrombus to lyse and remodel, but it is common to see residual thrombus on follow-up duplex ultrasound. It is important to be clear with patients that this is not at all unusual and does not necessarily portend a major problem. Most patients’ major concern is that the residual clot may come astray and cause problems, but after a couple of weeks any residual clot is firmly adherent to the vessel wall.

SUPERFICIAL VENOUS THROMBOSIS

Superficial venous thrombosis presents most commonly in either the saphenous trunks or varicose tributaries. Patients with superficial venous thrombosis are at risk of thrombus extension into the deep venous system, with the possible consequences of pulmonary embolism and post-thrombotic syndrome. Up to 25% of patients may have contiguous involvement of the deep system at the time of presentation, and in another 10%, the thrombus may go on to extend after initial presentation.

The first point to make regarding

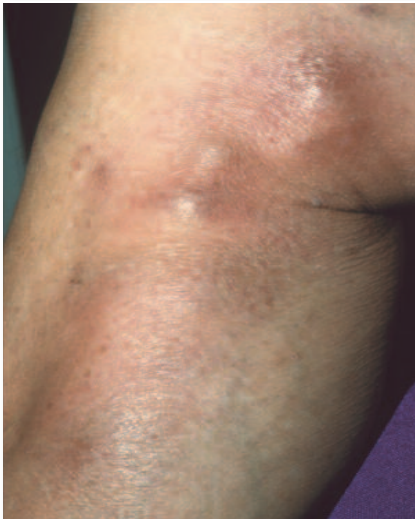


Figure 2. Redness and inflammation associated with superficial venous thrombosis in a patient with varicose veins.

superficial venous thrombosis relates to the deep venous system. The nomenclature of the lower limb venous system can be misleading in that the superficial femoral vein is in fact part of the deep system, not the superficial system (see Figure 1). There are several well-documented cases where a clinician noted that the superficial femoral vein was thrombosed and therefore decided that no treatment was necessary as the thrombosis only involved a superficial vein. There are moves to change the nomenclature of this vein but in the meantime vigilance for this issue will always be well rewarded. Occasionally an imaging report will be unclear, and it is then always worth checking with the performing sonographer or the reporting radiologist.

Another important point about superficial venous thrombosis is that the significant inflammatory component to the presentation (redness, swelling and heat) is due mainly to chemical inflammation rather than infection (Figure 2). Traditionally the condition has been known as 'thrombophlebitis', although some

clinicians prefer 'phlebothrombosis'. Superficial venous thrombosis is generally the preferred terminology these days. Unless the patient has had recent instrumentation of the vein in the form of an injection or infusion (and even then), the risk of infection is small and, therefore, antibiotics have no place in the treatment of this condition.

The clinical concerns in people presenting with superficial venous thrombosis are similar to, although not exactly the same as, those in people with calf vein thrombosis. The most obvious concerns to the patient are the inflammatory symptoms. More importantly, there is the risk in these patients of thrombus extension to involve the deep venous system (Figure 3), in much the same way as occurs with calf vein thrombosis. Another important point is that clinical examination will almost always underestimate the involvement of the venous system, and duplex ultrasound should be relied on to assess this in the first instance.

Treatment

The most obvious goal of treatment for patients with superficial venous thrombosis is relief of symptoms. This can be achieved with anti-inflammatory medication and topical treatments.

Given the three issues of clinical underestimation of involvement, possible extension and possible DVT, anticoagulation is now advocated as the first-line treatment for superficial venous thrombosis. A recent (2010) major study has confirmed the safety and efficacy of this approach.⁵ Some authorities consider superficial venous thrombosis as part of the spectrum of venous thromboembolism and treat it accordingly.⁶ In patients with a high risk of bleeding or with a very small (less than 5 cm) localised thrombosis, a conservative approach with topical anti-inflammatory treatments and surveillance is acceptable. Otherwise, treatment with a prophylactic dose of LMWH or fondaparinux for six weeks is recommended, with escalation to

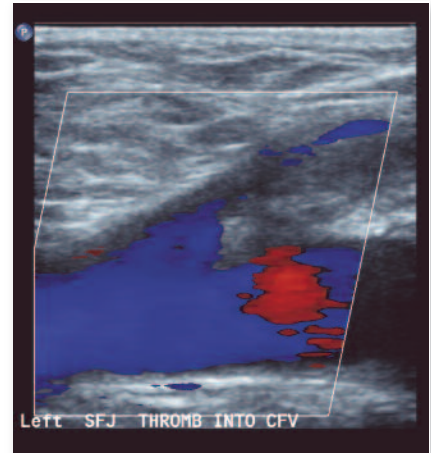


Figure 3. Duplex ultrasound demonstrating thrombosis of the greater saphenous vein extending to the junction with the common femoral vein with high risk of further extension/embolisation.

full anticoagulation if there is thrombus extension or the thrombus is adjacent to the deep venous system.

Surgery has traditionally been advised in cases of superficial venous thrombosis where the proximal extent of the thrombosis is within 5 cm of the junction with a deep vein. Advocates of primary anticoagulation point out that an operation will contribute to further risk of venous thromboembolism in a patient who has already demonstrated a thromboembolic tendency. In addition, the use of anticoagulation deals with this risk, the risk of extension into the deep system and the risk of pulmonary embolism. Therefore, in this situation, there are probably few instances where surgery would be recommended as initial therapy. However, the vast majority of patients with superficial venous thrombosis will have varicose veins as their predisposing factor, and the risk of recurrence of their venous disease and the need for its definitive treatment should be discussed at some point. (In fact, superficial venous thrombosis in a person without varicose veins should at least prompt consideration of a search

for another cause, such as an occult neoplasm.) The risk of recurrent episodes of superficial venous thrombosis is high in patients with thrombosis of varicose tributaries, mandating early treatment of the underlying cause.

As with patients with calf vein thrombosis, the natural history of their thrombus should be discussed with patients with superficial venous thromboembolism early in the course of their treatment for the condition.

CONCLUSION

Calf vein thrombosis and superficial venous thrombosis are common presentations in clinical practice but clear guidelines are lacking regarding how best to care for patients with these thrombotic events, despite the well developed management guidelines for patients with DVT and/or pulmonary embolism. However, awareness of the natural history of thrombi, follow up with relevant investigations and early appropriate treatment leads to a good outcome in this group.

Although the novel oral anticoagulant rivaroxaban is listed on the PBS for the treatment of DVT, further research is required regarding its use in calf vein thrombosis and superficial venous thrombosis. At this point, anticoagulation with LMWH or fondaparinux is a safe and effective treatment for these venous thromboses. MT

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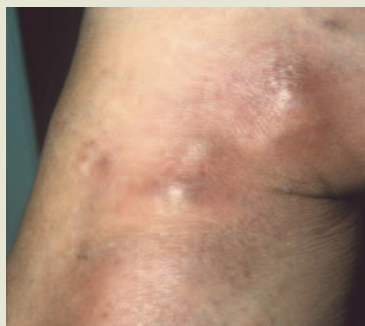
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COMPETING INTERESTS: Dr Robinson has received honoraria from Merck Sharp and Dohme for speaking at meetings.

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