Isolated pharmacomechanical thrombolysis using the Trellis system
GJ O'Sullivan

Introduction
While anticoagulation remains the current gold standard for treating acute deep vein thrombosis,¹ there is a growing body of evidence that rapid thrombus removal results in better short- and long-term outcomes.²⁻⁵ This is a practical guide to achieve rapid thrombus removal with isolated pharmacomechanical thrombolysis using the Trellis® peripheral infusion system.

Although it may sound obvious, it is surprising how often a supposedly 'acute' deep vein thrombosis is, in fact, chronic or acute-on-chronic. This may sound like a trivial distinction, but it has wide-reaching implications for treatment. Primarily, and fundamentally, thrombus older than 14–21 days becomes fibrin-depleted,⁶ so techniques to achieve fibrinolysis, on their own, are likely to fail.⁷

Previous episodes of cellulitis, bruising, cramping, heaviness, spider-vein development, and so on are important clues to make the physician consider the possibility that this presentation is not purely the result of an acute deep vein thrombosis.⁸

Patients rarely connect seemingly distant events with the acute problem. They may consider long-term unilateral or bilateral leg swelling as their normal state without realizing this often implies an episode of prior deep vein thrombosis and the current acute deep vein thrombosis reflects thrombosis of the veins peripheral to a stenotic or obstructive underlying lesion. This is most obvious with iliac vein compression syndrome,⁹ but there are other pathologies that may cause a similar venous stenotic lesion.¹⁰

In patients who have experienced a recent onset of cough or shortness of breath, including more chronic symptoms such as those ascribed to asthma, a computed tomography (CT) pulmonary angiogram should be performed as the initial part of the CT venogram.

General symptoms such as malaise or weight loss should prompt a search for a malignancy; in women, recurrent abortions together with a deep vein thrombosis would suggest a systemic pro-coagulant disorder.¹¹

Diagnosis
Ultrasound is used to diagnose most cases of lower extremity deep vein thrombosis, but more proximal lesions are frequently missed or underdiagnosed, due to the difficulty of visualizing the iliac veins and inferior vena cava.¹²⁻¹³ Even in skilled hands, and with slim patients, the iliac veins can be difficult to see.

CT venography is increasingly coming to the fore in this arena.⁹,¹⁴ The technique is beyond the scope of this chapter, but I view CT pulmonary angiography and CT
venography as essential in every patient, prior to considering any form of interventional deep venous therapy (Fig. 1).

Attention must be paid not only to filling defects in the pulmonary arteries suggestive of acute embolus, but also to the size of the proximal pulmonary arteries and the right ventricle. If either of these is enlarged, an echo may be prudent to assess the pulmonary arterial pressure and degree of functional right ventricular impairment; this is not an academic exercise, as elevation of the pulmonary arterial pressure is associated with a worse outcome.15

Inferior vena cava anomalies collateral formation, narrow calibre iliac veins, and low attenuation filling defects in swollen veins indicative of acute deep vein thrombosis are all revealed (Figs 2 and 3). In addition, CT venography allows the depiction of compressive lesions as well as the presence of tumours, which are themselves likely to make the patient hypercoagulable (e.g., colonic or pancreatic malignancy) (Fig. 4). Magnetic resonance venography can depict acute venous thrombosis and may allow timing of the age of the actual thrombus, but has not as yet found the same favour as CT in this arena. Catheter venography is reserved for the actual interventional procedure.

Figure 1. Axial CT scan with intravenous contrast at mid thigh level demonstrates thrombus in femoral veins, both superficial and deep.

Figure 2. CT scan at the level of the upper inferior vena cava demonstrates a small suprarenal inferior vena cava and an enlarged azygous vein.

Figure 3. Note small right external iliac vein compared with the left in a patient with an apparently acute right leg deep vein thrombosis.
Patient selection

The most successful results are obtained in patients with acute thrombus regardless of which technique is used. Based on a combination of history, ultrasound and CT venography, it is possible to select those patients who are likely to do best with specific techniques.

'Ideal patient'

The ideal patient is young, previously fit and active, and has a clearly defined precipitating event to provoke the venous thrombosis. There is no shortness of breath. There will be no positive family history, the left leg is more likely to be involved, and it will be significantly swollen.

Imaging will reveal a patent popliteal vein (on ultrasound, clearly compressible) with acute thrombosis on CT venography from the left common iliac vein down to the mid femoral vein in the thigh (Fig. 5). Note that malignancy is not a contraindication to aggressive catheter-based treatment.

Figure 4. Coronal CT scan demonstrates occlusive thrombus in the left common femoral vein. In addition, a large pelvic mass is evident.

Figure 5. Coronal CT demonstrates thrombus in inferior vena cava and left common iliac vein (see arrows).
'Less than ideal patient'

Each of the following increases the complexity of the case:

- Previous ipsilateral deep vein thrombosis.
- Imprecise onset of symptoms (more likely older thrombus).
- Presence of pulmonary embolism or elevated pulmonary arterial pressure.
- Thrombus in the inferior vena cava.
- Thrombus in the popliteal vein.
- Thrombus in all visualized calf veins.
- Age, infirmity, inability to move limb well.
- Recent gastrointestinal bleed.
- Renal impairment.

Note that these are not described as contraindications to treatment using the Trellis catheter, since there is a body of opinion which now believes there are no definite contraindications to the use of this specific technique.16–17

A thorough description of the advantages or disadvantages of the different techniques to remove/dissolve thrombus is beyond the scope of this chapter, but a brief description is in order.

Systemic thrombolysis is appropriate only for symptomatic pulmonary embolus with haemodynamic compromise.15 It has no place in the treatment of deep vein thrombosis as the bleeding rates are simply too high for it to be acceptable, and the thrombolysis does not reach the area of thrombus in significant concentration.7 Although it does lead to better rates of venous recanalisation than standard anticoagulation, it is nowhere near enough to be useful. Systemic thrombolysis, therefore, offers most of the risks with few of the rewards.

Catheter directed thrombolysis is well established in the treatment of symptomatic deep vein thrombosis.7,18,19 Based on the large United States multicenter registry,7 the major complication is of bleeding; major bleeds requiring transfusion or prolonging hospital stay occur in <10%. The risk of haemorrhagic stroke is less than 0.4%. I only employ this technique, in conjunction with Trellis, if there is extensive below-knee thrombus which is difficult to attack with Trellis (Table 1).

A brief summary of the various methods of mechanical thrombus dispersion mechanisms follows.

- Ultrasound-assisted: Ultrasound waves partially fragment and increase the surface area of thrombus, which can be attacked by the thrombolytic agent, thus shortening the time of treatment; slurry is aspirated (Ekos).20
- Rotational mechanical: A wire-driven nitinol fragmentation cage pulled slowly through the clot macerates and strips clot from the vein wall; slurry is aspirated (Arrow Trerotola).21
- Bernoulli effect: Saline jets powered at a high speed create a vacuum which draws thrombus through side holes of the catheter, fragmenting thrombus into microscopic pieces; slurry is aspirated (Possis Angiojet).22
- Isolated pharmacomechanical thrombolysis: Distal and proximal balloons largely confine slurry to the treatment area; a thrombolytic agent is stirred through the thrombus with a sinusoidal wire, increasing the surface area of thrombus that can be lysed; slurry is aspirated (Covidien Trellis).16
Isolated pharmacomechanical thrombolysis using the Trellis system • GJ O'Sullivan

Using ultrasound guidance and a micropuncture system (Angiodynamics, Queensbury, NY), access is gained percutaneously to the vein (preferably popliteal), a 5F sheath is inserted, and venography performed to delineate the area requiring treatment. As the thrombus is invariably occlusive at some level, contrast opacification more proximal to this point may be suboptimal. An angled Glidewire (Terumo, Tokyo, Japan) is inserted through the sheath together with a 65 cm Kumpe catheter (Angiodynamics). We manoeuvre the guidewire/catheter combination into the most caudal portion with occlusive thrombus and then repeat venography by gentle hand injection (Fig. 6). This delineates the extent of occlusive thrombus. The catheter/wire combination is then advanced into a proximal vein. Again, venography is used to confirm that this vein is free of thrombus. It is critical to identify the proximal extent of the thrombus so that the more cephalad Trellis balloon may be inflated here.

Table 1. Thrombolysis Technique. CDT, catheter directed thrombolysis; CT, computed tomography; IPMT, isolated pharmacomechanical thrombolysis; PMT, percutaneous mechanical thrombectomy

Trellis: detailed description of technique

Acute symptomatic above knee deep vein thrombosis

Inferior vena cava involvement
Pulmonary embolism on CT pulmonary angiography
Dilated right ventricle
Elevated right heart pressures

Yes – Inferior vena cava filter
No

Calf vein involvement

Yes
No

CDT

Accelerated CDT + Trellis (24h or less)

CDT from any calf vein or popliteal vein

Trellis from popliteal vein puncture – single session treatment

Completion manoeuvres including venous angioplasty and stenting – all patients
Depending on the clinical situation, and the most proximal position of the thrombus (e.g., in an iliofemoral deep vein thrombosis), access is gained up to the inferior vena cava, after which, a 260 cm Amplatz 0.035 inch wire is inserted. A 10F sheath is then inserted to accommodate the aspiration catheter and the commonly used larger size stents. (The newer Trellis catheter fits through a 6F sheath.) The patient is systemically heparinized with 5,000 units of intravenous heparin. The Amplatz wire is left with its tip in the inferior vena cava, and the Trellis catheter is inserted. Depending on the physical height of the patient, either an 80 cm or a 120 cm device is used (generally >1.7 m height requires a 120 cm long device). Either a 15 cm or a 30 cm infusion-length device is chosen, depending on the length of thrombus. Then the peripheral balloon, i.e., the one nearest the sheath, is inflated to an appropriate diameter. The central balloon is inflated in an area which does not contain thrombus. For example, in a patient with a left iliofemoral deep vein thrombosis, we inflate the balloon in the distal inferior vena cava just at its junction with the left common iliac vein. The balloon is pulled back gently while being inflated until it is well positioned in either the very distal inferior vena cava or the common iliac vein (Fig. 7). Although placement of the balloon in the distal inferior vena cava and gentle retraction is somewhat at variance with the manufacturer’s recommendations, we have found that this method works very well with iliofemoral deep vein thrombosis extending up to the inferior vena cava. I now treat cephalad to caudad, which is different from previous publications.16

Figure 6. Prone view of a left leg venogram shows absolute obstruction to the flow of contrast due to occlusive deep vein thrombosis in the left iliac venous system.

Figure 7. Balloons inflated in inferior vena cava and left common femoral vein are seen in a prone view.

Thrombolytic agent dosage

The Trellis catheter comprises two segment treatment lengths – 15 cm and 30 cm. We recommend that 5 mg tissue plasminogen activator is used with the 15 cm device, and
10 mg tissue plasminogen activator with the 30 cm device. These are diluted with an equal volume of normal saline and infused gradually over 5 minutes, as the device is activated.

The Trellis itself is an over-the-wire system which combines a mechanical element and an isolation segment (Fig. 8). Two balloons can be inflated distally in diameters ranging from 5–16 mm. A sinusoidal nitinol wire replaces the procedure wire and is Luer locked into position between the balloons. As the lytic agent is infused (only between the balloons), a motor is activated in the drive shaft to oscillate the wire at about 2000 rpm. The points of contact of the sinusoidal wire and the venous wall can be altered by shifting the transition point.\textsuperscript{16}

The total amount of tissue plasminogen activator used is a fraction of that used in catheter directed thrombolysis; in addition, there is very little systemic absorption as evidenced by no change in fibrinogen levels pre- and post-treatment.\textsuperscript{16}

Figure 8. Trellis system.

After a maximum of two passes of the device, repeat venography is performed through the sheath. In most cases, more than 90% of all thrombus is removed (Figs. 9a and b). The remaining thrombus is aspirated using either a detachable-hub sheath

Figure 9. (a) Prone view of left iliac and common femoral vein demonstrating occlusive thrombus in the left external iliac vein with absolute obstruction in the left common iliac vein overlying a hip prosthesis. (b) Post Trellis there is Grade III thrombolysis of the involved segment, but persistent obstruction to flow in the left common iliac vein.
Following isolated pharmacomechanical thrombolysis with the Trellis device and aspiration thrombectomy, an underlying stenosis requiring stenting is invariably identified (Fig. 11). It is essential that both the superior and inferior aspects of the stent lie in normal vein ('flow to flow'). Often this means common femoral vein to inferior vena cava — a distance of 15–24 cm. It also is critical that large enough stents are used to attain a diameter post balloon dilatation of a minimum 12 mm — and often up to 20 mm (Fig. 12). This is considerably larger than the size of iliac artery stents

![Figure 10](image)

**Figure 10.** Significant quantities of fresh thrombus may be aspirated once it has been sufficiently thrombolysed and macerated.

![Figure 11](image)

**Figure 11.** Post Trellis and aspiration thrombectomy, further adherent thrombus has been removed and the underlying causative stenotic lesion due to iliac vein compression syndrome is revealed.
Figure 12. (a) 14 mm balloon dilatation of left common iliac vein stenosis due to compression from overlying right common iliac artery. (b) Completion venography following Trellis, aspiration thrombectomy, stenting and balloon dilatation reveals rapid in line flow through the previously obstructed segment into the inferior vena cava. Skin to skin time 54 minutes.

typically employed. Wallstents may show considerable expansion and shortening over 24–48 hours. Crossing the inguinal ligament is not an issue; the stents have good radial expansile force and maintain luminal patency despite acute angulation (Fig. 13).

Figure 13. (a) Self-expanding stents have considerable radial force and excellent flexibility which is essential crossing joints. Here a triathlete flexes her knee to her shoulder post thrombolysis and stenting. (b) Excellent in line flow is seen through this acutely angled stent.
Completion venography should demonstrate rapid in-line flow from a popliteal venous injection which clears within a maximum of 5 seconds.

Pneumatic compression boots (Covidien Healthcare, Loughlinstown, Ireland) are used overnight after the procedure. These boots cause periodic and rhythmic calf compression to simulate walking and encourage more rapid blood flow. Patients are encouraged to mobilise as aggressively as possible, which is achieved by the active involvement of physiotherapy.

Use of inferior vena cava filters

I would recommend the use of temporary or permanent retrievable filters in the following situations:

1. Pulmonary emboli on a recent CT pulmonary angiogram.
2. Dilated/dysfunctional right ventricle or elevated pulmonary artery pressures on echo.
3. Thrombus within the inferior vena cava.

The first two situations are straightforward, and although these are not standard indications (as the first would merely be an indication for prolonged anticoagulation), they have proven correct in my experience.

Thrombus within the cava is a special situation, and a higher than usual position of the filter may be necessary (e.g., a permanent retrievable supra-renal inferior vena cava filter). Occasionally, despite caval thrombus, a filter may not be required if the supra-renal cava is of particularly small calibre.

Assuming satisfactory resolution of the underlying pathology, the filter may later be removed.

In the unlikely event that Trellis and aspiration thrombectomy do not achieve Grade III lysis, then accelerated catheter directed thrombolysis may be needed (in approximately 20% of the cases in my experience). It is not necessary for patients to be in an intensive care unit environment but, unfortunately, this is standard in many institutions. The patient does need to be on bed rest. All patients should wear thigh-high compression stockings (with holes cut in the back for the catheters), and pneumatic compression boots are of proven benefit. The frequency of blood draws for estimation of haemoglobin, fibrinogen, fibrin degradation products, and activated partial thromboplastin is probably in the 6–8 hour range. A significant fall in fibrinogen levels from pre-treatment levels is a warning sign that the dose of tissue plasminogen activator needs to be reduced.

The dose of tissue plasminogen activator is not set in stone, but a total hourly dose of 0.5–1 mg tissue plasminogen activator is standard. I might aim for a slightly higher dose if ‘accelerated’ catheter directed thrombolysis (24 h or less) is being used (e.g., 1–2 mg/h) whereas a lower dose (0.25–0.5 mg/h) appears more appropriate for longer duration ‘standard’ catheter directed thrombolysis.

Post operative care

Following completion of treatment Class 2 thigh high stockings are mandatory (probably for 6 months) and pneumatic compression boots are useful for the first night. I always obtain a Colour Doppler ultrasound on day one post treatment to confirm venous patency. On the handful of occasions there has been acute rethrombosis, it
is critical to reoperate immediately, as the thrombus is at its freshest and easiest to treat. Usually, this is due to missing an underlying stenosis or not allowing for stent shortening.

All patients require anticoagulation: 3 months for patients with deep vein thrombosis treated by Trellis, and 6 months for patients with deep vein thrombosis and pulmonary embolism treated by Trellis. (In the case of deep vein thrombosis + pulmonary embolism treated by catheter directed thrombolysis, 3 months is probably reasonable as some thrombolytic agent invariably goes systemic during the 2–3 days of the procedure; there is no proof or trial to back this up however.)

I obtain a CT venogram at 6 weeks to assess patency and review the patient in the clinic after that.

Results

Because the device is relatively new, reports of experience are somewhat limited.16,17,27,28 Using Society of Interventional Radiology reporting standards for deep vein thrombosis lysis (grade I = <50%; II = 50%-95%; III = >95% clot clearance),25 grade I lysis occurred in only one of twenty two patients (n = 1/22; 4%), grade II lysis clearance occurred in 18/22 limbs (82%); three limbs demonstrated grade III lysis (14%). Since then, over 100 cases of deep venous thrombosis treatment using the Trellis catheter have been carried out at our institution, and the degree of Grade III lysis achieved at single session treatment has now improved to over 85% while the time taken per case has fallen to under 100 minutes skin to skin.

Other reports demonstrate similarly successful results,29–30 but are often combined with overnight catheter directed thrombolysis. I feel the Trellis on its own can be successfully employed for single session deep vein thrombosis therapy. The only exceptions to this are with bilateral lower limb and inferior vena cava thrombus, and extensive below knee thrombus. Both of these usually require catheter directed thrombolysis in addition to Trellis, but the use of the Trellis radically shortens the duration of infusion. For any single session method, it is a requirement of the device to puncture into a vein with flow, and the Trellis is no exception.

Conclusion

Acute symptomatic above knee deep venous thrombosis may be successfully treated using isolated pharmacomechanical venous thrombolysis using the Trellis peripheral infusion catheter with a high degree of technical success and minimal complications. In a small proportion of cases, overnight catheter directed thrombolysis may be required post Trellis as an adjunct.

Summary

- Acute symptoms may signal a chronic or acute-on-chronic deep vein thrombosis.
- CT venography is essential in diagnosis of deep vein thrombosis lesions that are difficult to see on ultrasound.
• Contraindications to the isolated pharmacomechanical thrombolysis procedure are relative rather than absolute.
• Isolated pharmacomechanical thrombolysis limits systemic exposure to tissue plasminogen activator in a clot-clearing procedure that may take less than 100 minutes ‘skin to skin’.
• Use of inferior vena cava filters is advised in certain cases.
• Post-procedure pneumatic boots and anticoagulation regimens are similar to those of other percutaneous mechanical thrombectomy techniques.
• Isolated pharmacomechanical thrombolysis with the Trellis catheter may be used to treat deep vein thrombosis with a high degree of technical success and minimal complications.

References


