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A contemporary overview of the management of acute ilio-femoral deep vein thrombosis; why, how, and where next?

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Unprovoked acute deep vein thrombosis (DVT) is a common problem, affecting around 50 to 100 per 10000 people.[1,2] A significant number of these (20%) will involve the iliac veins or inferior vena cava. The symptoms of acute DVT are well described and include, sudden onset of swelling, pain, redness and difficultly mobilising. On occasion the extent of venous congestion can be so severe it threatens the limb, a phenomenon termed *phlegmasia*.

The cornerstone of DVT management irrespective of the location, is anticoagulation, elevation, and compression of the affected limb.[3,4] These initial steps can improve acute symptoms but the rate at which symptoms resolve with these measures alone is variable. In the medium to long-term, all patients with a DVT are at risk of developing persisting symptoms such as swelling, skin changes, venous eczema, venous claudication, and ulceration; termed post-thrombotic syndrome (PTS), and occurs after approximately 50% of all DVTs.[5] These symptoms have a significant negative impact on quality of life for which there is no 'cure'.

In the case of ilio-femoral or ilio-caval DVT despite best medical management, the frequency and severity of PTS is higher with more extensive thrombus.[5] Furthermore, younger patients are at greater risk[6] of long-term sequelae. This has stimulated research into early thrombus removal to attempt to improve patient outcomes. Landmark randomised controlled trial evidence exists to support early intervention in these patients to reduce the thrombus burden with a view to reducing the medium- to long-term severity of post-thrombotic syndrome.[7,8] However, there are some conflicting findings, and the evidence does leave some questions unanswered[9] mostly due to criticism of the inclusion criteria, procedural 'best-practice' and follow-up. There are also controversies in the descriptors used for the location of the DVT; proximal and distal DVT which was used to define above or below the knee which is not commonly accepted among DVT interventionalists where the inguinal ligament is often the anatomical landmark used as a discriminator for intervention. This obviously introduces heterogeneity when trying to interpret these studies and assimilate the evidence. As such, identifying patient groups who would most benefit from intervention becomes a challenge. Newer concepts of ascending *versus* descending DVT have been poorly explored to date but could provide a platform for future case selection.

Nonetheless, over the last fifteen years or more there has been steady incremental development in the clinical expertise and the available technology to support the intervention for acute-iliofemoral or above DVT. These technologies have expanded considerably and present novel solutions for the patients.

In attempt to keep up with the evolving landscape, the 2018 NICE guidelines support the use of a variety of technologies but recommended these should be reviewed by local governance structures, audit and be accompanied with adequate patient information. By 2021, the European Society of Vascular Surgery guidelines have recommended that *early thrombus removal is more effective than anticoagulation alone in preventing PTS and recommend that early removal strategies should be considered in patients with symptomatic iliofemoral thrombosis*.[10] Lately, in 2023, the Society of Interventional Radiology have issued a consensus statement[11] supporting the role of thrombus removal in acute iliofemoral DVT to reduce post-

thrombotic syndrome, reduce acute symptoms and embolic risk. Influential publications such as these have further bolstered the awareness of intervention for iliac vein DVT.

As a result, within the UK, the active management of acute iliofemoral DVT is gaining traction. The technological advances and manufacturer competition has seen a plethora of devices available for the treatment of DVT, all with their nuances and with good safety and efficacy profiles.

There are broadly four types of intervention available, all requiring endovascular or interventional skill set, delivered under radiological guidance, under local anaesthesia or with conscious sedation. However, general anaesthesia may be preferable when stents placement is required.

'Catheter thrombolysis': a traditional DVT management technique, reliant on thrombolytic agents to dissolve the clot. The efficacy data is good,[12,13] and the bleeding risk is small but to be effective, thrombolysis must begin soon after presentation as it is only effective on fibrin rich thrombus which occurs for up to 14 days and often repeated trips to the x-ray suite are required. It should be avoided in those with bleeding risks, such as in the post-operative setting or following neurosurgery. In the ATTRACT Study no stroke or death from bleeding was reported.[7]

'Aspiration thrombectomy': there are a variety of aspiration-based devices which work to remove the thrombus under a vacuum, in a single treatment session. Non-comparative data suggest it is effective at thrombus removal with a good safety profile,[14] although some data suggests blood-loss can be a challenge with these techniques. These are also generally applied to acute thrombus within the two-week window.[15]

'Rheolytic devices': these combine mechanical fragmentation, pulsatile thrombolysis delivery and aspiration of the thrombus material. Registry data demonstrate[16] this is an effective technique to remove thrombus, but the timing is key as older thrombus becomes harder to clear. Concerns over renal damage that can occur due to haemolysis have been reported[17] and this limits the volume of thrombus that can be cleared.

Mechanical thrombectomy: These newer lysis-free devices have promising registry data.[18] They work by utilising a collapsible coring element and basket to remove and capture thrombus material. The interventions offer the option of treating patients with a wider time-range of presentation, thereby increasing the patient cohort that can be treated. Furthermore, the single-session approach without thrombolysis increases some of the patient eligibility. An industry supported global multi-centre randomised control trial is underway to support the early registry data (Figures 1-4).

All these interventional options offer a comprehensive armamentarium for the treatment of a wide range of DVT presentations and present clear technical solutions. However, DVT management requires careful attention to detail. This includes, but is not limited to, careful patient selection, engagement with the thrombosis MDT for anticoagulation advice, thrombosis risk management, audit of outcomes and good governance, coupled with appropriate patient counselling regarding treatment expectations. Such specialised care requires dedicated teams with considered regional pathways, all requiring appropriate resourcing and infrastructure.

The future of acute ilio-femoral or -caval DVT intervention is certainly a rapidly changing and fast-moving landscape. There are several future challenges that need some consideration to ensure practice is equitable, safe, evidence based and sustainable.

At present there is some inequity across the country with regards to the availability of such options for management. The Vascular Society of Great Britain and Ireland Provision of Services for Vascular Disease (2021) suggested that selected patients with ilio-femoral DVT and or life or limb threat should be offered

acute DVT treatment. An unpublished survey (by the Vascular Endovascular Research Network) has suggested that there are only a handful of UK vascular centre's regularly intervening and therefore capable of delivering such therapies. This presents a potential post-code lottery for access for this treatment with subsequent variation in patient safety and outcomes.

It could be argued that without clear evidence of efficacy and safety, practice should be limited to higher volume centres with the appropriate multi-disciplinary expertise to review, consider and then counsel patients for intervention and the aftercare. Research is a potential challenge for the management of the acute proximal DVT, with industry driving the latest RCT the hope is that this will provide some irrefutable data to support the already available cohort, registry and trial data for acute iliac DVT intervention. The broader vascular and interventional community is inundated with funded research projects and will have to consider how to deliver these competing interests to time and ultimately for the benefit of patient care. Any new DVT-related research is likely to be challenging as past trials in acute DVT treatment have proved difficult to complete due to a reluctance for patients to be randomised and a high screen failure rate – ATTRACT for example screened 50 patients for every one enrolled.

If the rate of expansion in the field continues with more and more interventions being performed for acute iliofemoral and/or caval DVT[19] there will be future challenges with regards to wide-spread training. At present deep venous interventions are not part of vascular or interventional radiology core curricula. This does present an interesting debate over the provision of appropriate training. Should this be limited to enthusiasts and Fellowship systems or should curricula for the relevant teams be expanded to include these interventions? What is clear is that the without the support of industry and the reliance on enthusiastic clinicians the awareness of the problem of iliofemoral DVT would not be as widespread.

In summary, the management of acute iliofemoral or ilio-caval DVT is an example of a rapidly changing healthcare field, and a clear demonstration of how technological advances can improve patient care. Through the development of considered and appropriate clinical pathways, intervention can help to alter the clinical sequalae after acute DVT by reducing the severity of PTS and improving recovery. Careful governance, standardisation and training are essential to ensure that equitable, high-quality care is offered nationwide.

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Figures

Figure 1. Set up in endovascular theatres.

Figure 2. thrombus removed after mechanical thrombectomy.

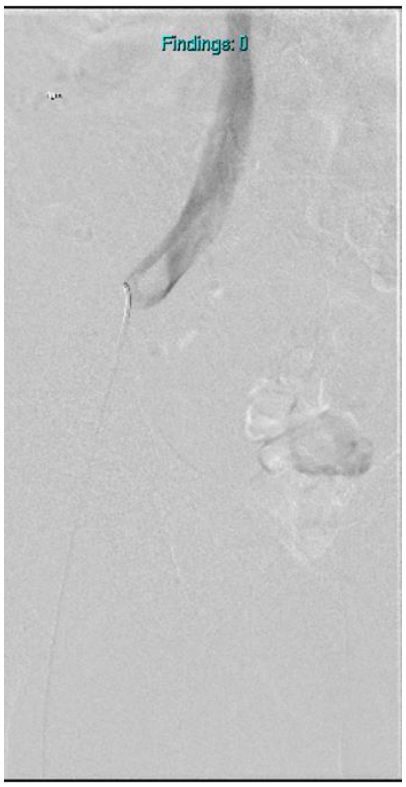

Figure 3. Large DVT before thrombectomy.

Figure 4. Venogram showing patency restored by mechanical thrombectomy.