Management of Iliofemoral Deep Vein Thrombosis: A Hybrid Approach

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Abstract

Despite recent innovations in clot lysis technology, management of acute ili-femoral Deep Vein Thrombosis (DVT) remains a challenge worldwide. We revisit the work of a previous generation of vascular surgeons who created a temporary Arteriovenous Fistula (AVF) in combination with a surgical thrombectomy, to maximize blood flow through the newly revascularized vessel. Since this time, surgical thrombectomy along with the use of a temporary AVF, has been superseded by endovascular techniques: namely Catheter-Directed Thrombolysis (CDT) and Pharmacomechanical Thrombolysis (PMCT). We review the evolution of the management of ili-femoral deep vein thrombosis, specifically examining the trials which investigate temporary AVF with surgical thrombectomy. Furthermore, we describe the surgical technique of creating a temporary AVF, including how to avoid venous hypertension and how to facilitate closure if required. Finally, in the age of hybrid techniques, we propose that a temporary AVF could be used in combination with current thrombus removal techniques to possibly lower the risk of recurrent thrombosis and complications such as post-thrombotic syndrome.

Keywords: Abdominal compartment syndrome; Complicated intra-abdominal infection; Intestinal perforation; Ruptured abdominal aortic aneurysm

Introduction

Despite recent innovations in clot lysis technology, management of acute ili-femoral Deep Vein Thrombosis (DVT) remains a challenge worldwide. Long-term complications of proximal DVT include Postthrombotic Syndrome (PTS), which is characterized by chronic limb heaviness, pain, swelling, paraesthesia, pruritis and pigmentation changes [1,2]. PTS affects between 23-43% of patients and has been shown to have a significant negative impact on quality of life and a large economic burden on the wider community [3-7]. Early active treatment to remove thrombus has been shown to result in better outcomes, including lower rates of venous valve dysfunction [8], recurrent DVT [9] and PTS [10-12].

Pathology Of Thrombus Formation: Virchow’s Triad

Our current understanding of thrombus formation as a triad of dysfunction of vessel wall, blood flow and blood components was first hypothesized by Rudolf Virchow in 1856 [13]. Firstly, thrombosis can result from an imbalance in the coagulation cascade as a result of inherited and/or acquired molecular defects [14]. Secondly, disruption of blood flow slows the inflow of clotting factor inhibitors, prevents activated clotting factors from dispersing, and allows platelets to come into contact with the endothelium. Thirdly, endothelial injury exposes the thrombogenic sub-endothelial extra-cellular matrix, leading to adhesion and activation of platelets, and the exposure of tissue factor, which activates the coagulation cascade [15]. Importantly, whereas once the endothelium was thought of as a “cellophane wrapper” covering the vasculature, we now understand that endothelial cells play a vital regulatory role in the balance between haemostasis and blood fluidity - even a small perturbation can activate the endothelial cells, with tumour necrosis factor suppressing the formation of thrombomodulin and inducing the expression of tissue factor, tipping the balance in favour of haemostasis and thrombosis [16].

Thrombus-related damage to the endothelial-lined venous valves more than doubles the risk of both valvular incompetence and recurrent venous thrombosis [9,17]. Although the exact mechanism of the damage is unclear, it is likely that early valvular incompetence is due to inflammation and recanalization. Conversely, late-onset valvular incompetence is likely due to persistent outflow obstruction and chronic venous ambulatory hypertension. Interestingly, there is also an increase in valvular incompetence in the surrounding non-affected veins, which is likely to be a result of venous hypertension causing dilatation of the vessel and the separation of the valve leaflets [17]. In the investigation of both chronic thrombosis and valvular incompetence, and suspected acute thrombosis in the lower limb, Doppler and B-mode ultrasound studies have been shown to be highly accurate, objective, reproducible and cost effective [18,19].

Current Management: Anticoagulation

For an unprovoked DVT of the proximal lower limb, current guidelines of the American College of Chest Physicians recommend early oral anticoagulation and continuation of parenteral anticoagulation with unfractionated heparin, low-molecular weight heparin or fondaparinux for five days or until the International Normalized Ratio (INR) is 2.0 or above for more than 24 hours [12]. For both first and recurrent unprovoked events, the guidelines recommend three months of anticoagulation therapy for patients with a high bleeding risk and extended anticoagulation therapy for patients with a low to moderate bleeding risk [12]. If a patient has a contra-indication to anticoagulation, the use of an inferior vena cava filter is recommended [12]. Adjuvant therapies such as mechanical thrombectomy, Catheter-Directed Thrombolysis (CDT) and Pharmacomechanical Thrombolysis (PMCT), act to reduce the thrombus load and restore blood flow.
A Review of Clot Lysis Techniques

Surgical thrombectomy for acute iliofemoral venous thrombosis was first reported by Läwen in 1937 [20]. By the 1960s, it was being widely performed in the US [21,22]. A damming study published by Lansing and Davis in 1968 [23], however, virtually stopped the practice. In this study, the authors reviewed 17 patients who had undergone surgical thrombectomy for acute DVT five years prior. They reported leg swelling in 16 of 17 patients and incompetent valves in the affected area in 15 of 17 patients. Their study was critically flawed: only 17 of the original 34 study participants had been interviewed; and the venography was performed with patients in a supine position, which cannot accurately assess incompetency of valves [20]. Despite this, very few surgical thrombectomies were performed in the United States after this report; the practice continued only in a few European centres.

From the late 1960s, systemic thrombolysis was being trialled for the management of iliofemoral DVT. With this procedure, patients received an intra-venous infusion of Urokinase (UK), Streptokinase (SK) or recombinant tissue Plasminogen-Activator (rt-PA) for three to seven days. Most trials comparing systemic thrombolysis to conventional anticoagulation reported more cases of complete or partial resolution of clot with systemic thrombolysis, with approximately 50 – 70% of patients having some degree of lysis [24]. These positive results were offset by an increased risk of bleeding - the risk of major bleeding 13.2% compared to 3.5% in patients treated with heparin [25].

Catheter-Directed Thrombolyis (CDT) developed in response to the unacceptably high risk of bleeding reported with systemic thrombolysis. In CDT, a smaller dose of thrombolytic agent is injected via a catheter device directly into the thrombus. Trials have shown positive results in terms of clot lysis and a more acceptable risk of major bleeding and mortality [26,27]. Newer catheter devices, such as the Trellis-8 Peripheral Infusion System™ (Covidien Inc., Mansfield, MA) and the AngioJet Rheolytic Thrombectomy System™ (Medrad Interventional - Bayer, Minneapolis, Minnesota) have an additional mechanical function, which acts to macerate the clot, thus increasing contact of lytic agent with clot and accelerating clearance [28-30]. The Trellis-8 Infusion Catheter System™ consists of a single-use catheter device with two occlusive balloons (5-16 mm) and a sinuosidal-shaped nitinol ‘dispersion’ wire connected to a pump via a Luer-Lok [31,32]. The two occlusive balloons are inflated proximally and distally to the target area, isolating the infusion of the thrombolytic agent. When in use, the dispersion wire rotates, causing the catheter to oscillate at 500-3500 rpm, dispersing the lytic agent and mechanically disrupting the clot. After which, fragments of the clot are suctioned out. The AngioJet™ system includes a single-use, fenestrated catheter, connected to a pump set and a drive set [33]. As the catheter is passed through the thrombus, a high-power jet of thrombolytic agent is pulsed through the catheter fenestrations, causing an area of low pressure at the catheter tip. After thirty minutes, the catheter is again passed through the clot, aspirating the macerated clot via the efferent tube. Current evidence for these devices, termed Pharmacomechanical Thrombolyis (PMCT) is sparse - a large multi-centre randomized controlled trial (ATTRACT) is ongoing [30,34].

Is the Management of Stasis Standing Still?

Despite extensive evidence linking stasis to the development of thrombosis, intervention to maximise blood flow in the management of iliofemoral DVT is the least studied. Normal blood flow is laminar, in which platelets travel centrally in the vessel lumen, separated from the endothelium by a slower flowing clear zone of plasma. Stasis disrupts laminar flow, bringing platelets into contact with the endothelium. It also prevents dilution of activated clotting factors, retards the inflow of clotting factor inhibitors and permits the build-up of thromb, thereby promoting endothelial cell activation, resulting in local thrombosis and leukocyte adhesion. A recent study has shown that there is a significant increase in plasma interleukin-6 (IL-6), endothelin-1 (ET-1) and Angiotensin II (ATII) in acute peripheral venous congestion [35]. The endothelial-lined bicuspid valves in the venous system are also exposed to disturbed blood flow and reduced shear stress during the normal valve cycle [36]. In fact, blood has been shown to remain stagnant for up to 27 minutes in the valve sinuses in the leg, which becomes relatively hypoxic, inflaming the underlying endothelial cells [37,38].

Clinical evidence for stasis as a contributor of DVT is manifold: there is a higher incidence of DVT in the paralyzed leg compared to the active leg in hemiplegic patients; institutionalisation – either in hospital or nursing home residences - is attributable for 59% of DVT in community; and hospitalized medical and surgical patients experience an equal proportion of DVT [39]. Given the causal role of stasis in thrombus formation, it follows that blood flow is vital in preventing thrombus formation and re-thrombosis post-clot clearance. Therein lies an opportunity to maximize treatment of acute iliofemoral DVT - to actively increase blood-flow by constructing a temporary arteriovenous fistula (AVF) distal to the target site.

Arteriovenous Fistulae and Iliofemoral DVT

Following the Lansing and Davis study, some European centres continued to perform surgical thrombectomies for acute iliofemoral DVTs [40-45]. The following two decades saw considerable change in the practice: superior non-invasive imaging; the introduction of the Fogarty catheter; the combination of a temporary AVF with thrombectomy; intra-operative venography; and a longer post-operative course of anticoagulation [23].

European studies at the time were small and non-randomised. Juhun et al. [46] reviewed 77 lower extremities after surgical thrombectomy and temporary AVF for acute DVT and reported 84% vessel patency with valvular competence at 80% at 5 years, dropping to 56% at 10 years.

Plate et al. [47] followed-up thirty patients ten years after a prospective, randomised study comparing surgical thrombectomy/ temporary AVF and conventional anticoagulation treatment with anticoagulation alone. In the intervention arm, leg swelling was seen in six patients (46%), and lower limb ulceration in one (8%), compared to 12 (71%) and three (18%) patients respectively in the conventional arm. These results were not statistically significant given the small numbers. In the same study, radionuclide angiography showed that the iliac vein was more commonly occluded following conservative treatment (59%) than surgical intervention (17%) (p<0.05). The researchers concluded, therefore, that venous thrombectomy improves patency and could potentially reduce venous reflux and post-thrombotic sequelae.

Swedenborg et al. [41] evaluated 17 patients after venous thrombectomy combined with a temporary AVF - the primary surgery was unsuccessful in two patients who had chronic occlusion of iliac veins. At three months, 14 patients had a patent iliac vein. After a
mean follow-up of 38 months, eight patients had a patent iliac vein, eight had partial reconstitution, and three had an occluded iliac vein.

Thirty patients were evaluated post-venous thrombectomy with temporary AVF by Meissner [48]. In this study, the temporary AVF was closed 8 to 12 weeks after its creation. Three patients died during early the post-operative period: one due to cardiogenic shock secondary to massive myocardial infarction, and two from septic shock. Of the remaining 27 patients, complete patency of iliofemoral veins was achieved during the operation in all, and none of the patients had signs of re-thrombosis within 30 days. At one year post-fistula closure, moderate leg swelling was noted in 16 patients, however no patients experienced ulceration or re-thrombosis.

In summary, these studies, although small, yielded consistently favourable results. Despite this, the use of a temporary AVF with thrombectomy is still out of favour along with surgical thrombectomy. In an age of hybrid solutions, a temporary AVF could be beneficial when used in combination with CDT/PMCT to minimize the potential for re-thrombosis.

Arterio-Venous Fistulae: Surgical Technique

An AVF can be constructed by end-to-side anastomosis using the end of proximal saphenous vein or preferably a large proximal branch of the saphenous vein anastomosed to the side of the proximal superficial femoral artery or profunda femoris with the anastomosis limited to 3.5 to 4.0mm in diameter [49]. Then, a wrap of polyethylene or silastic can be placed around the saphenous AVF. Finally, a large permanent monofilament suture is looped around the wrapped vein and clipped with approximately 2 cm left in the subcutaneous tissue to guide future dissection if operative closure of the AVF is necessary.

While some researchers have reported closure of the AVF by percutaneous balloon occlusion [50-52], most patients do not require closure as flow through the small AVF diminishes with time because of neo-intimal fibroplasia [49]. If closure of the AVF is necessary, it is commonly performed after 4-8 weeks [46,47]. The common femoral vein pressure is measured before and after the AVF is opened. The venous pressure should not increase when the AVF is flowing - elevation of venous pressure on opening AVF dictates the need for proximal iliac vein re-evaluation for residual stenosis or obstruction and correction of any proximal lesion. In cases of persistent increased pressure, the AVF should be constricted to decrease flow and normalise pressure [53] or even ligated to prevent iatrogenic venous hypertension.

Conclusion

The management of acute iliofemoral deep vein thrombosis is constantly evolving. Clot removal techniques, such as surgical thrombectomy and thrombolysis, have been shown to be superior to anticoagulation therapy alone, resulting in decreasing rates of postthrombotic syndrome and DVT recurrence. Nonetheless, there is still a considerable disease burden in the community. In the search for better patient outcomes, we revisit the work of a previous generation of vascular surgeons who created a temporary AVF in combination with a surgical thrombectomy to promote blood flow through the newly re-vascularized vessel. A number of small studies support their work, presenting consistently positive results. We propose that a temporary AVF could be beneficial when used in combination with anticoagulation therapy and CDT or PMCT. A temporary AVF is a simple technique to perform with minimal risk to the patient, and great potential to prevent re-thrombosis and PTS. We believe further investigation is warranted to test this hypothesis.

References


