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Techniques in Vascular and Interventional Radiology

Catheter-Directed Interventions for Acute Iliocaval Deep Vein Thrombosis

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Acute deep vein thrombosis (DVT) is associated with significant morbidity in the form of acute limb-threatening compromise from phlegmasia cerulea dolens, development of the postthrombotic syndrome (PTS), and even death secondary to pulmonary embolism. Initial therapy for DVT is anticoagulation, which inhibits thrombus propagation but lacks the thrombolytic properties to facilitate active thrombus removal. The existing thrombus burden can cause increased venous hypertension from occlusion as well as damage to venous valves by initiating an inflammatory response, which can ultimately result in PTS in up to half of patients on anticoagulation. The manifestations of PTS include leg pain, swelling, lifestyle-limiting venous claudication, skin hyperpigmentation, venous varicosities, and, in rare cases, venous stasis ulcers. Furthermore, patients with iliocaval DVT and large, free-floating thrombus are at an increased risk for pulmonary embolism despite adequate anticoagulation. Early attempts at thrombus removal with surgical thrombectomy or systemic thrombolysis or both demonstrated reductions in the incidence of PTS but were of limited utility owing to their invasiveness and increased risk of bleeding complications. New minimally invasive endovascular therapies, such as pharmacomechanical catheter-directed thrombolysis, have been proposed, which focus on rapid thrombus removal while decreasing the rate of bleeding complications associated with systemic therapy. This article provides an overview of the current pharmacomechanical catheter-directed thrombolysis protocol utilized at the Mount Sinai Hospital for acute iliocaval DVT.

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Introduction

Over 900,000 venous thromboembolism (VTE) events, consisting of deep vein thrombosis (DVT) and pulmonary embolism (PE), occur annually in the United States.[1] Current first-line therapy for VTE is anticoagulation, which prevents further thrombus formation. However, some studies have shown thrombus propagation in almost 40% of patients on anticoagulation therapy.[2] In addition, anticoagulation alone does not facilitate active removal of the existing thrombus burden, which in the acute setting, can result in phlegmasia cerulea dolens, extensive swelling of the involved extremity with subsequent development of arterial insufficiency, compartment syndrome, venous gangrene, and amputation. DVT may also cause increased venous hypertension secondary to obstruction as well as valve incompetence or reflux from damage incited by an inflammatory reaction to the thrombus. These factors are considered to be the underlying mechanisms for the development of the postthrombotic syndrome (PTS), which can occur in up to 50% of patients on the standard anticoagulation therapy.[3] PTS is characterized by a multitude of symptoms, such as leg swelling, heaviness, aching, lifestyle-limiting venous claudication, skin hyperpigmentation, venous varicosities, and, in rare cases, venous stasis ulcers.[4]

Acute PE occurs in 1 per 1000 people in the general population every year and is the number one cause of in-hospital deaths with a mortality rate of 30% in untreated patients resulting in up to 180,000 deaths yearly.[5] Patients with thrombotic disease that extends into the inferior vena

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cava (IVC) are at an increased risk for PE despite anticoagulation, particularly when there is extensive proximal or free-floating thrombus.[6]

Rapid thrombus removal has been proposed to reduce the incidence of both PE and PTS. Initial efforts with surgical thrombectomy and systemic thrombolysis showed improved venous patency and reduced PTS rates but were limited owing to their invasiveness and higher rates of complications associated with both minor and major bleeding.[7-9] Recent advances in vascular imaging and endovascular technology have resulted in minimally invasive catheter-directed interventions, such as catheter-directed thrombolysis (CDT) and pharmacomechanical catheter-directed thrombolysis (PCDT).

CDT involves placement of a multi–side-hole catheter directly into the thrombus, with subsequent infusion of a thrombolytic agent. This approach has several theoretical advantages to systemic thrombolysis, namely the ability to attain a high intrathrombus drug concentration while reducing bleeding complications. Recent results from the catheter-directed venous thrombolysis study demonstrated a significant reduction in the incidence of PTS in the CDT treatment arm vs the traditional anticoagulation group at 2 years (41% vs 56%, $P = 0.047$).[10] Limitations of CDT include lengthy thrombolytic infusions times (mean of 55.2 hours) in an intensive monitored setting (intensive care unit or step-down unit).

PCDT refers to the combination of mechanical thrombectomy and CDT, which augments the rate of thrombus removal while reducing thrombolytic agent dose and infusion times. Observational studies have demonstrated promising results with PCDT[11-14]; however, at this time no multicenter, randomized, controlled trial demonstrating the long-term efficacy of PCDT exists. The acute venous thrombosis: thrombus removal with adjunctive catheter-directed thrombolysis trial is an ongoing National Institute of Health-sponsored, phase III, multicenter randomized clinical trial that seeks to compare patients receiving PCDT plus standard therapy to standard therapy alone, measuring the cumulative incidence of PTS over 2 years.[15] At this time, the study has enrolled approximately 521 of the planned 692 patients. Currently established PCDT uses either the "power-pulse" or "isolated thrombolysis" techniques. Power pulse employs the AngioJet rheolytic thrombectomy system (Bayer, Warrendale, PA), which uses high-pressure saline jets to create a strong negative pressure gradient (Bernoulli effect) that draws the thrombus to the catheter inflow windows, where it is captured, fragmented, and ultimately aspirated through the catheter. Isolated thrombolysis uses the Trellis peripheral infusion system (Covidien, Mansfield, MA) to deliver the thrombolytic agent directly into the clot, which is then circulated within the clot by an oscillating wire between proximal and distal occluding balloons. The vibration caused by the wire and dispersion of thrombolytic agent macerates the thrombus. The proximal balloon is deflated and the thrombus is aspirated (distal balloon maintained to reduce risk of embolization).

The current PCDT protocol at the Mount Sinai Hospital utilizes a single-day treatment without the need for intensive monitoring during thrombolysis in patients with acute iliofemoral and iliocaval DVTs. This article provides an overview of this protocol in addition to discussion of appropriate patient selection, preprocedure planning, technical considerations, as well as appropriate follow-up.

Clinical Evaluation

DVT should be suspected in patients who present with symptoms of lower-extremity swelling, pain, and erythema. Obtaining pertinent clinical history is important to determine whether a patient has risk factors for VTE, such as a history of VTE, recent hospitalization, lower-extremity orthopedic surgery, prolong immobilization, advanced age, trauma, inherited thrombophilias, pregnancy or postpartum status, and myocardial infarction. Physical examination may demonstrate discoloration, warmth and edema of the involved extremity, and in rare cases a palpable cord may be present. Pretest probability for DVT can be assessed with the modified Wells score, which stratifies patients into low (3%), intermediate (17%), and high (75%) likelihood groups.[16] Laboratory tests such as serum D-dimer levels may also be helpful, which have a high negative predictive value for DVT.

Ultrasound has emerged as a highly sensitive and specific noninvasive imaging modality for patients with clinical presentations suspicious for DVT (Fig. 1).[17] Patients with proximal DVT should undergo further evaluation with computed tomography or magnetic resonance venography to fully assess thrombus extent and to determine if an underlying structural lesion is present (eg, May-Thurner).

Indications for PCDT

As previously mentioned, no long-term outcome data from a multicenter randomized clinical trial are yet available to characterize the subgroup of patients with DVT who would most greatly benefit from intervention. A recent review by Vedantham recommended a "…highly individualized approach to patient selection" with careful consideration given to the severity of the clinical presentation, the symptom duration, life expectancy, activity level, the risk of bleeding, the location of the occlusion, and the patient's desire or ability to undergo such a procedure.[18]

Patients with severe acute DVTs associated with limb-threatening compromise or patients with worsening IVC thrombosis or both despite anticoagulation therapy should be considered for urgent PCDT, unless they are at significantly increased risk for bleeding. Patients with proximal DVT or with worsening DVT symptoms or thrombus extension despite anticoagulation may be considered on an elective basis if they are at low risk for bleeding complications. Favorable outcomes have been seen in patients with acute symptomatic DVT (less than 2 weeks) as well as those with structural lesions (eg, May-Thurner), which would be amenable to stenting.[2,19]

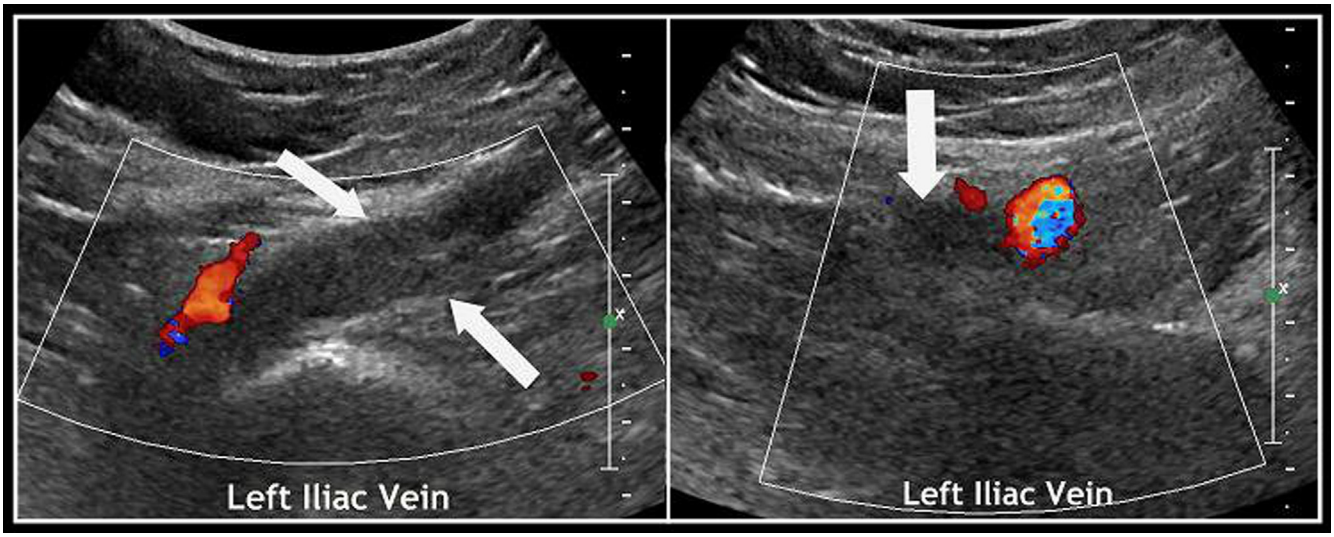

Figure 1 Ultrasound demonstrates occlusive thrombus within a distended left common iliac vein. (Color version of figure is available online.)

Preprocedure Planning

Adequate preparation is important to optimize patient outcomes and minimize periprocedural complications. Before intervention, patients should undergo imaging with computed tomography or magnetic resonance venography to delineate the location and extent of thrombus as well as to determine if any underlying structural lesion is present (Fig. 2). If there is extension or free-floating thrombus within the IVC, it may be reasonable to place an IVC filter before initiation of PCDT to reduce PE risk. Imaging also provides information concerning the most proximal patent

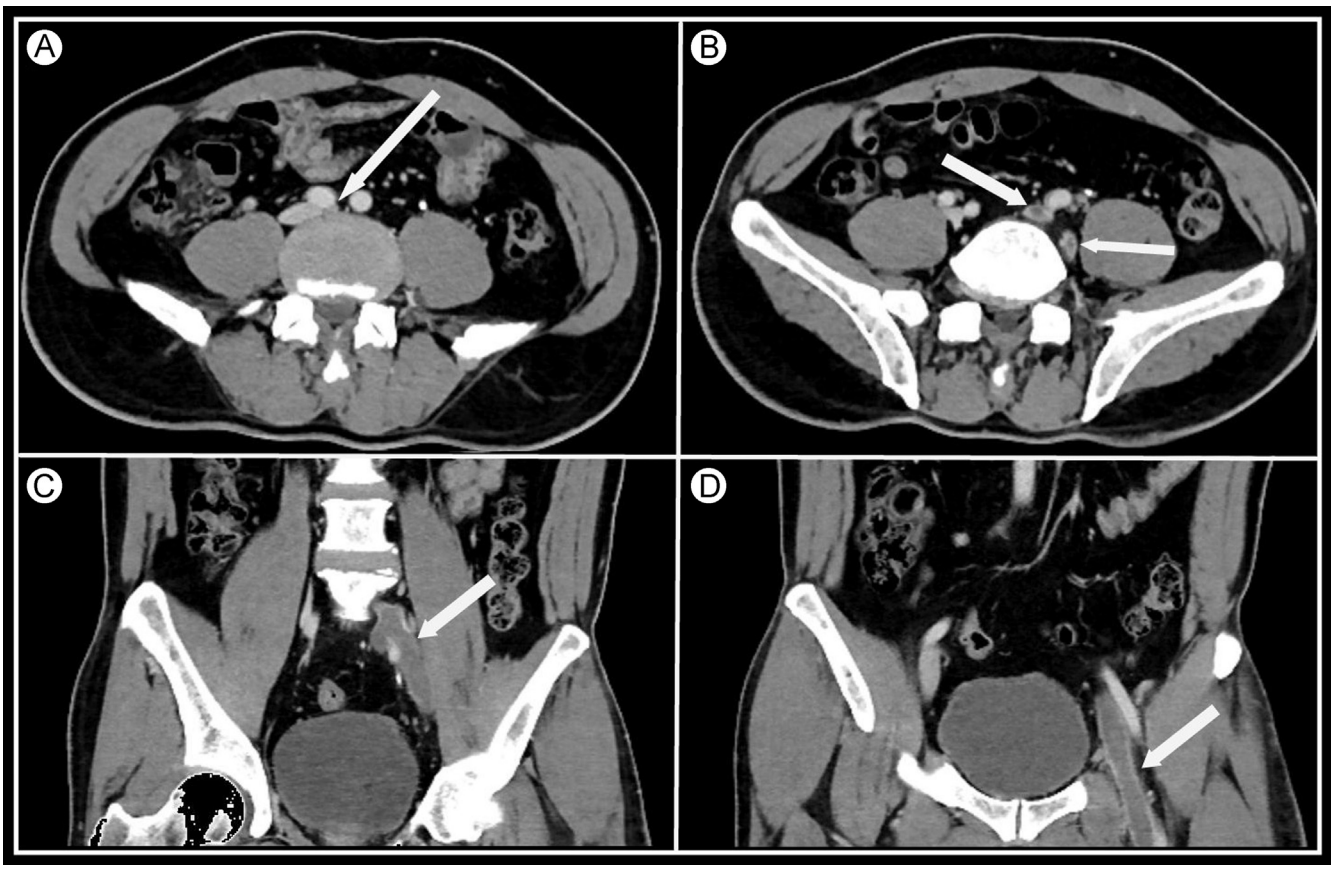

Figure 2 (A) Axial CT venograph demonstrates extrinsic compression of the left common iliac vein by the overlying right common iliac artery, compatible with May-Thurner syndrome. (B) Axial CT venograph shows intraluminal filling defects within the left internal and external iliac arteries. (C) Coronal CT venograph demonstrates intraluminal filling defect within the left common, internal, and external iliac veins. (D) Additional coronal image demonstrates inferior extension of thrombus.

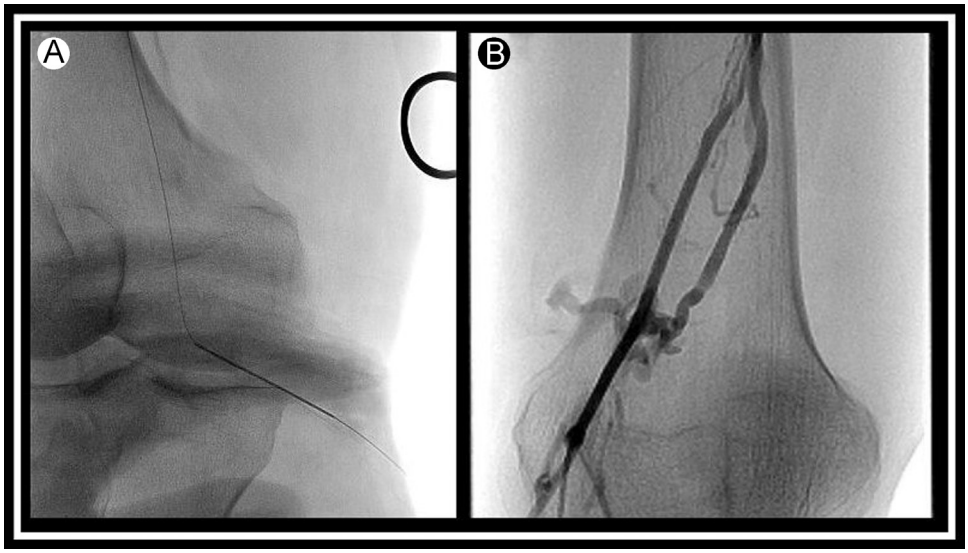

Figure 3 (A) After obtaining access to the left popliteal vein under ultrasound guidance, the guidewire is advanced through the popliteal vein. (B) Popliteal venograph after placement of 8-F vascular sheath.

venous segment, as well as which may be the preferred access site (most frequently the popliteal vein and less commonly the posterior tibial or jugular vein).

Early initiation of anticoagulation should be undertaken to inhibit further thrombus formation in the interim period between diagnosis and PCDT. Patients who are on warfarin therapy should be converted to unfractionated or low-molecular-weight heparin before initiating therapy for easier periprocedure anticoagulation control. Patients should also be wearing intermittent pneumatic compression devices during and after intervention. Intermittent pneumatic compression devices have been shown to improve vascular inflow as well as increase endogenous fibrinolytic activity.[20]

Aggressive hydration should be started before PCDT for renal protective measures to reduce the risk of acute tubular necrosis from hemolysis as well as reduce the risk for contrast-induced nephropathy.

Required Equipment

The standard Mount Sinai PCDT protocol typically employs the following devices:

- Micropuncture kit (21-gauge needle, 5-F sheath, 0.018 in guidewire);
- hydrophilic 0.035 in guidewire;
- stiff 0.035 in support wire;
- angled-tip multipurpose catheter used to cross DVT;
- 8-F vascular sheath; and
- AngioJet rheolytic thrombectomy system (Bayer, Warrendale, PA).

PCDT Protocol

The patient is brought into the angiosuite and placed into prone position, and the involved extremity is prepared and draped in sterile fashion. Under ultrasound guidance, the most proximal patent vein segment is accessed with micropuncture technique (Fig. 3) with placement of a 5-F sheath. Subsequently the 0.035 in guidewire is advanced through the thrombus into the IVC using the standard catheter and guidewire technique and the 5-F sheath is exchanged for an 8-F vascular sheath. The crossing wire is then exchanged for a stiff support wire. Venography is performed to assess extent of the thrombus.

A 6-F AngioJet catheter is then advanced over the wire into the thrombus. After the placement of the AngioJet, we employ the "power-pulse" technique, which consists of the catheter being slowly retracted back into the sheath, while pulse spraying a bolus of diluted thrombolytic agent (12-25 mg of tPA diluted into 50-100 mL of saline) over the length of the clot. During the pulse-spray infusion, the aspiration port of the AngioJet catheter is placed in "closed" position to prevent aspiration of the thrombolytic agent. The lytic agent dwells over the clot for approximately 30-45 minutes. The AngioJet catheter is then reintroduced over the wire and 2 full passes are made with the outflow port "open" to attempt thrombus aspiration.

Venography is then performed (Fig. 4), and based on the appearance of the clot, any of the following decisions may be made : (1) to perform balloon maceration, (2) to perform mechanical thrombectomy, (3) to initiate CDT transferring the patient to the recovery room during infusion, or (4) a combination of these techniques. Residual disease after these options may be further treated with venoplasty and stenting as needed (Fig. 5).

Completion venography is then performed to demonstrate improved patency, and all the catheters and wires are removed and manual compression is performed until hemostasis is achieved.

This single-session procedure was initiated at the Mount Sinai Hospital in September 2005 and has remained our standard technique.

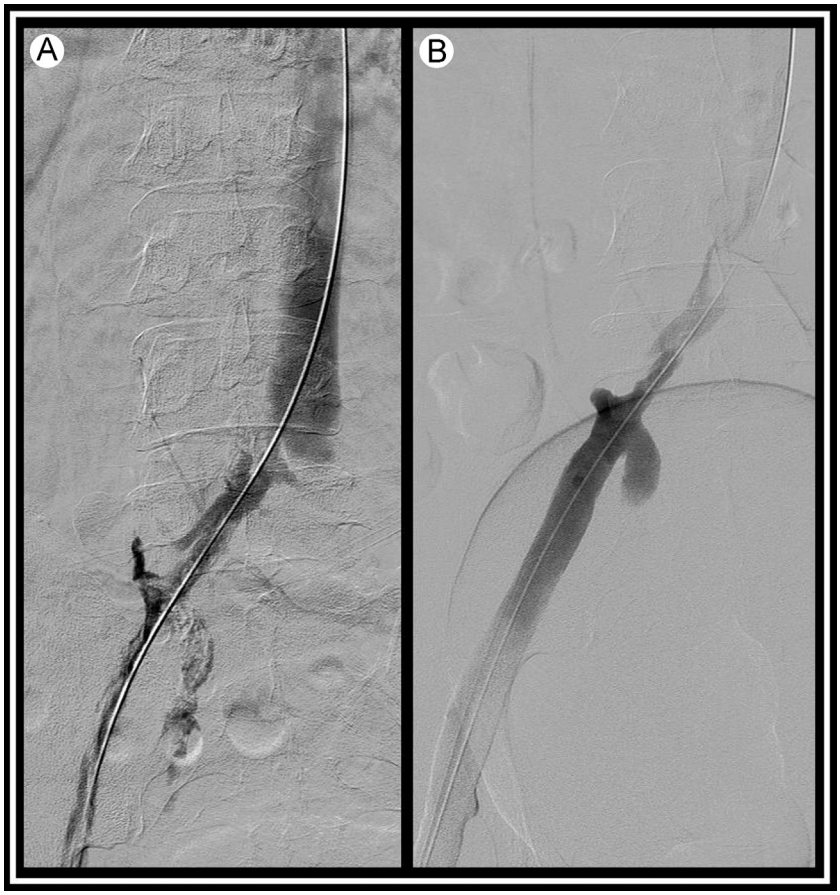

Figure 4 (A) Venograph demonstrates intraluminal fillings defects within the left common, internal, and external iliac veins. (B) Post-PCDT venographs demonstrate improved flow through the internal and external iliac veins. Persisting stenosis is seen in the proximal left common iliac vein, suggestive of May-Thurner lesion.

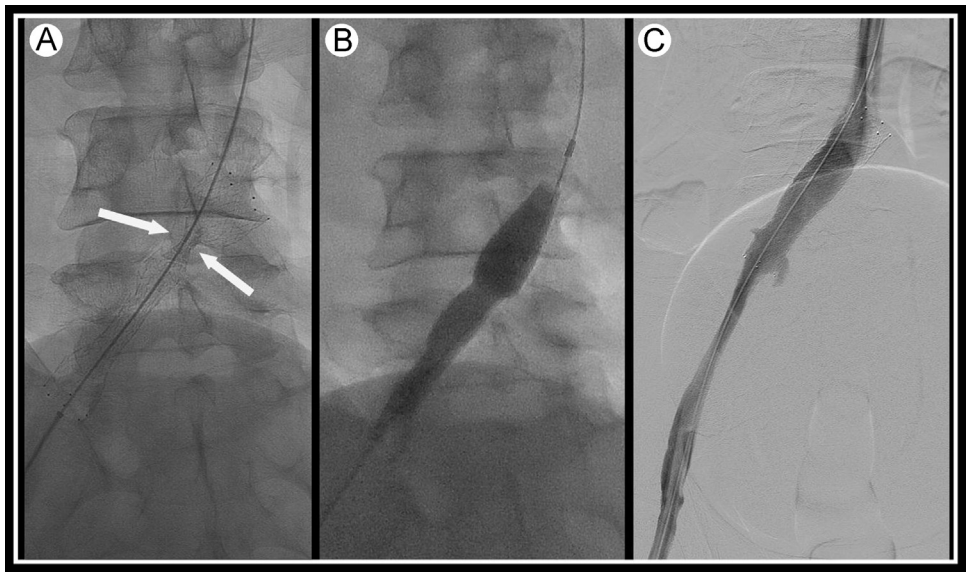

Figure 5 (A) Stent placement within the proximal left common iliac vein. A "waist" is noted within the stent. (B) Balloon dilatation is performed throughout the stent. (C) Poststent venoplasty demonstrates no residual narrowing within the stent.

Potential Technical Considerations

Appropriate preprocedure planning and imaging as well as careful patient selection is essential to minimize the incidence of unanticipated technical challenges. However, even with proper planning some unavoidable challenges may be encountered. A few of the more common occurrences experienced at our center are described later.

In cases of extensive occlusive or chronic DVT, there may be trouble in passing the guidewire beyond the occlusion. In certain instances, the back end of a hydrophilic wire may be used for recanalization; however, this technique carries risks of vessel dissection or rupture and should only be performed by experienced operators.

During lysis and thrombus aspiration with the AngioJet catheter, it is necessary to maintain good wall apposition. This can be difficult to maintain when thrombus is encountered in larger vessels, namely the iliocaval segments. In these instances using curved 8-F guide catheters (cobra, hockey stick, or multipurpose) can improve AngioJet wall surface contact via the "rapid lysis" technique, as was previously described by Garcia[21] and Garcia et al.[22]

Stenting should be used judiciously and primarily for central (iliocaval) short-segment (<10 cm) structural lesions exposed by thrombolysis. Precise stent placement may be difficult to perform in structural lesions at or near the IVC. In these cases, intravascular ultrasound can be used to provide further information regarding relative positioning of the stent as well as to verify that the stent has completely conformed to the venous wall. Stent placement in mobile areas, such as the common femoral vein as it crosses the femoral head, should be reserved for patients with long-term poor outflow from the thigh, as they may become prone to fracture and can subsequently obscure potential emergency venous access sites.

Periprocedural Complications

Published observational studies of PCDT have shown low complication rates compared with traditional CDT.[11-14] The most common periprocedural complication is bleeding, which occurred in approximately 3%-5% of patients. To reduce the risk of bleeding at the access site, use of ultrasound guidance is mandatory to avoid nearby arterial structures as well as using the smallest possible sheath; we typically use 8 F. If bleeding is noted at the access site, the thrombolytic agent should be stopped or reduced and hemostasis should be attempted with compression or sheath upsizing or both. If these measures are successful, then the thrombolytic infusion may be restarted at a lower dose with close serial examinations to ensure bleeding does not recur. If major bleeding occurs elsewhere, then the thrombolytic infusion should be stopped. At this time, physician discretion will dictate the need to obtain cross-sectional imaging and potentially stop heparin infusion as well.

Late complications primarily consist of reocclusion. It is crucial that in the postprocedure setting patients maintain therapeutic anticoagulation levels and are compliant with the use of compression stockings. If amenable, these patients can be retreated with repeat thrombolysis and venoplasty or stent placement, if a structural lesion is identified.

Clinical Follow-Up

After completion of the procedure, patients should be kept on therapeutic anticoagulation, instructed to ambulate early, and given compression stockings for daily use. For postprocedure anticoagulation therapy, low-molecular-weight heparin is often used for at least 30 days. Patients changed to oral anticoagulation therapies should be closely monitored and maintained at therapeutic levels. IVC filters that were placed should be removed within a short period of time to reduce risk of complications associated with long-term filter placement (thrombosis, IVC penetration, and migration).

Patients are usually seen approximately 1, 6, and 12 months after the procedure for clinical and ultrasound duplex evaluation. During clinical visits, it is important to encourage compliance with anticoagulation and compression stockings as well as to encourage ambulation or activity.

Anticoagulation should be maintained for at least 3-6 months in uncomplicated cases of PCDT who have no underlying risk factors for hypercoagulable states. Patients with predisposing factors for thrombosis may require longer anticoagulation, based on the underlying disease process.

Expected Outcomes

Until the 2-year follow-up data of PTS rates from the acute venous thrombosis: thrombus removal with adjunctive CDT trial are available, limited information on long-term outcomes can be gleaned from a handful of observational studies. These studies have documented patency rates of up to 75%-85% at 1 year; however, many were limited by suboptimal patient follow-up data.[11,12,14,23] It is commonly accepted that patients with acute central DVT or underlying structural lesions or both, who are amenable to stenting, have better outcomes compared with those with chronic peripheral lesions. As was noted before, close postprocedure patient follow-up and strict compliance with anticoagulation and compression stockings is imperative for favorable outcomes.

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