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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]