Interventional Management of DVT: Top 10 Technical Tips

Approaches, techniques, and preprocedure considerations for successful interventional management of DVT.

BY VINIT B. AMIN, MD; ROBERT H. SIEGELBAUM, MD; AARON M. FISCHMAN, MD; AND ROBERT A. LOOKSTEIN, MD

Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common cardiovascular disease in the United States after myocardial infarction and stroke.[1] The incidence of acute DVT is approximately 70 to 100 out of 100,000 people each year, with more than 100,000 to 300,000 cases annually in the United States.[2,3] Acute PE has an annual incidence of approximately 1 per 1,000 people in the general population, with a mortality rate of approximately 30% in untreated patients.[4]

Although VTE can be asymptomatic, its sequelae can include severe morbidity from postthrombotic syndrome (PTS), death from acute pulmonary embolus, or, less commonly, limb loss (venous gangrene, phlegmasia cerulea dolens). VTE is also associated with a significant economic burden. The cost of treating a single VTE event is between $10,000 and $16,000 per person, with a total United States annual expense of more than $2 billion.[5] A study by Guanella et al found that more than half of the total financial burden associated with VTE was attributable to missed work days, transportation costs for medical visits, home attendants, and other ancillary expenses.[6]

PTS is characterized by myriad symptoms such as leg swelling, heaviness, aching, lifestyle-limiting venous claudication, skin hyperpigmentation, venous varicosities, and venous stasis ulcers in rare cases (Figure 1).[7,8] Although not completely understood, the underlying mechanism is thought to be twofold: (1) venous hypertension caused by incomplete clearance of the obstructing thrombus and (2) valve incompetence/reflux from direct valve damage by an inflammatory response to thrombosis.[9] PTS has been reported in as many as half of all patients on standard anticoagu-

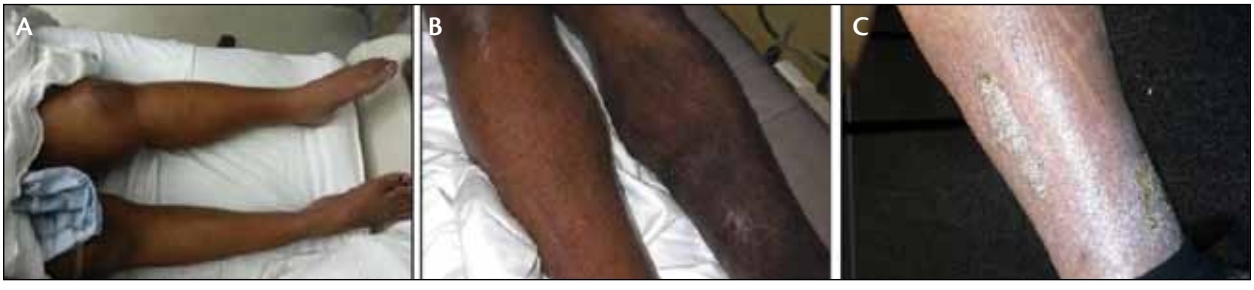

Figure 1. Manifestations of PTS. Unilateral leg swelling (A), hyperpigmentation (B), and venous stasis ulcers (C).

lant therapy alone for acute proximal lower extremity DVT, with rates of 25% seen in patients receiving both anticoagulation and elastic compression stockings.[10] PTS has been shown to have a detrimental effect on quality of life due to symptom severity. A 2008 study demonstrated that patients with moderate symptoms reported quality-of-life scores lower than those previously reported for conditions such as diabetes, arthritis, and chronic lung disease; those who reported severe symptoms had quality-of-life scores lower than those with chronic angina and congestive heart failure.[11]

Rapid thrombus removal has been shown to reduce the occurrence of valve reflux and has been suggested to improve venous flow.[12] A prospective randomized study of patients with acute iliofemoral DVT demonstrated improved venous patency and reduced PTS at 10 years in patients who underwent surgical thrombectomy and anticoagulation versus those who received anticoagulation alone.[13] Less-invasive alternatives, such as systemic thrombolysis, have also been studied. Two trials comparing the effect of systemic thrombolysis versus traditional anticoagulation determined that patients in the thrombolysis group had decreased rates of PTS; however, these trials also demonstrated higher rates of complications associated with both minor and major bleeding.[14,15]

ADVANTAGES AND LIMITATIONS OF CATHETER-DIRECTED THROMBOLYSIS

Advances in noninvasive vascular imaging and endovascular technology, as well as improved endovascular technique, have resulted in an emerging role for interventionists in the management of DVT. Catheter-directed thrombolysis (CDT) has several theoretical advantages to traditional systemic thrombolysis, including the ability to attain a high intrathrombus drug concentration while reducing the overall thrombolytic agent dose and treatment times, leading to fewer bleeding complications and decreased hospitalization length.[16] Standard protocols for CDT involve image-guided placement of a multisidehole catheter directly into the venous thrombus, which is then connected to an infusion of thrombolytic agent.[17] Some centers have replaced the standard multisidehole catheter with the EkoSonic infusion catheter system (Ekos Corporation, Bothell, WA) to enhance drug dispersion with low-power ultrasound energy, the efficacy of which is still under study.[16] After successful thrombolysis, any identified venous obstructive lesions are treated with balloon venoplasty with or without stent placement. Significant limitations of CDT include the long infusion time (typically 1–3 days), as well as the need for a closely monitored setting during infusion, such as an intensive care unit or step-down unit with serial laboratory measurements (fibrinogen, hemoglobin, partial thromboplastin time, platelet count). Four studies have compared CDT plus anticoagulation to anticoagulation alone, the most notable being the recent Catheter-Directed Venous Thrombolysis (CAVENT) study.[18] This multicenter randomized controlled trial of 189 patients demonstrated a reduced incidence of PTS in the CDT treatment arm at 2 years (41% vs 56%; $P = .047$). Major bleeding complications were more frequent in the CDT treatment group (three vs zero); however, none of these patients had long-term sequelae.

PHARMACOMECHANICAL CDT

The term *pharmacomechanical catheter-directed thrombolysis* (PCDT) refers to the combination of CDT with percutaneous mechanical thrombectomy.[16] This dual mechanism of action enhances the efficiency and rate of thrombus removal while improving safety by reducing drug dose and infusion times. Recent PCDT protocols have shortened endovascular DVT therapy to a single 1- to 3-hour on-table procedure session without the need for longer thrombolytic infusions and ICU monitoring. Several observational studies have shown successful implementation of PCDT,[19-22] but at this time, no multicenter randomized controlled trials have demonstrated the long-term effects of PCDT. The currently ongoing Acute Venous Thrombosis: Thrombus Removal With Adjunctive Catheter-Directed Thrombolysis (ATTRACT) trial is an NIH-sponsored, phase III, multicenter, randomized, open-label, assessor-blinded, parallel two-arm, controlled clinical trial. This study will randomize 692 patients to receive PCDT plus standard therapy versus standard therapy alone and will measure the cumulative incidence of PTS over 2 years.

Currently established PCDT uses either the "Power Pulse" or "isolated thrombolysis" techniques. Power Pulse employs the AngioJet rheolytic thrombectomy system (Bayer, Warrendale, PA) to deliver and disperse the thrombolytic agent by a powerful pulse-spray injection. After bathing the clot in the thrombolytic agent, the AngioJet catheter aspirates the softened thrombus fragments. Isolated thrombolysis uses the Trellis peripheral infusion system (Covidien, Mansfield, MA) to deliver the thrombolytic agent directly into the clot. The agent is then circulated within the clot by an oscillating wire.

PCDT PROTOCOL

The current PCDT protocol utilized at the Mount Sinai Hospital and Memorial Sloan-Kettering Cancer Center uses the Power Pulse technique, in which the

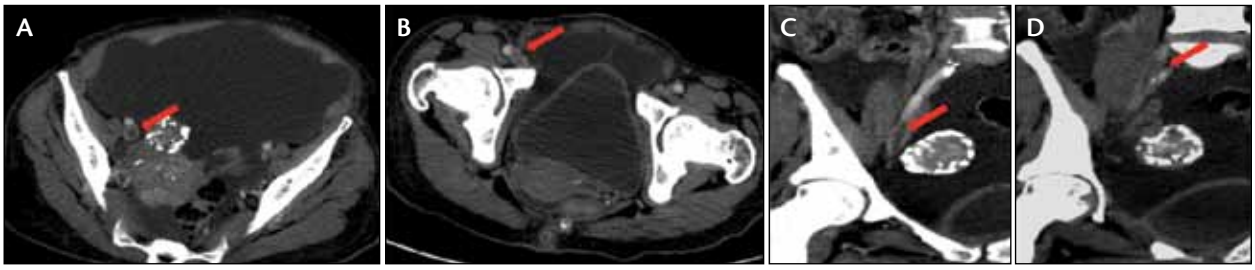

Figure 2. Axial (A, B) and coronal (C, D) images from CT venography show extensive right iliofemoral DVT in this patient with chronic liver disease.

AngioJet rheolytic thrombectomy catheter is placed into the thrombus. After placement, the catheter is 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.[23,24] During infusion of the thrombolytic agent, the aspiration port of the AngioJet catheter is clamped to prevent aspiration of the thrombolytic agent. After administration, the clot is bathed in the lytic agent for 30 to 45 minutes. The AngioJet catheter is then reintroduced, and two full passes are made to aspirate the thrombus. Venography is then performed, and based on the appearance of the thrombus, one may (1) perform balloon maceration, (2) initiate CDT, (3) perform directed mechanical thrombectomy with the AngioJet catheter in thrombectomy mode, or (4) use a hybrid of these techniques. Residual disease is treated with aggressive venoplasty and stenting as needed.

PCDT has been successful at our institutions in select patients with acute lower extremity DVT. The following section discusses techniques and procedural pearls used by the authors during PCDT for DVT.

1. Preprocedure CT Venography to Delineate the Extent of Disease

Preprocedure vascular imaging aids in the assessment of thrombus extent, as patients diagnosed with more proximal acute thrombus may potentially derive greater benefit from PCDT (Figure 2). In addition, CT helps to determine the location and number of access sites based on location and extent of the clot, as well as determining preprocedure filter placement in cases where the clot extends into the inferior vena cava (IVC).

2. Anticoagulate Early

Early anticoagulation inhibits further thrombus formation and allows for partial clearance of thrombus by endogenous plasmin.[25,26] Attaining and maintaining therapeutic anticoagulation is important in the interim period between diagnosis and PCDT. Current quality improvement guidelines recommend the concomitant use of anticoagulation during catheter-directed therapy based on empirical data from the published literature.[27] Patients who are already on warfarin therapy are converted to unfractionated or low-molecular-weight heparin before initiating therapy for easier periprocedure anticoagulation control. For postprocedure anticoagulation therapy, low-molecular-weight heparin is often used for at least 30 days. Cancer patients may require low-molecular-weight heparin due to the challenges of using warfarin in this population. A hematology consultation should be considered.

3. Initiate Kidney-Protective Hydration and Monitor Urine Output

Patients undergoing thrombolysis are at risk of developing acute kidney injury. Free heme protein released during hemolysis (an expected occurrence after use of the AngioJet device) can overwhelm the resorptive capacity of the proximal renal tubules, resulting in acute tubular necrosis. Additionally, patients undergoing venography are at risk for contrast-induced nephropathy (CIN), a leading cause of acute kidney injury.[28] Sodium bicarbonate infusions alkalinize the urine, reducing the renal tubular toxicity of hemoglobin and decreasing the risk of CIN.[29,30] Aggressive hydration protocols are used both during and after PDCT procedures to decrease the risk of kidney injury.

4. Venous Access Sites

Previous studies of catheter-based thrombolysis have described the internal jugular vein, common femoral vein, popliteal vein, posterior tibial vein, and pedal veins as potential access sites.[31,32] At our institutions, the preferred approach has been to select the most proximal patent vein segment. In most patients, this is typically the popliteal vein or, less commonly, the posterior tibial vein. The presence of adequate inflow is criti-

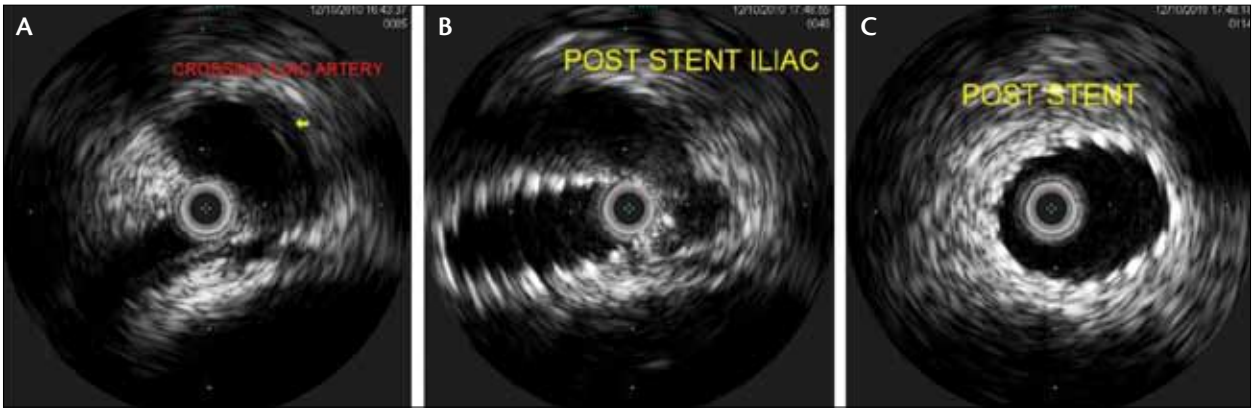

Figure 3. IVUS showing a May-Thurner lesion with right iliac artery crossing over and compressing the left iliac vein (A). IVUS-guided stent placement demonstrates improved left iliac vein patency (B, C).

cal for maintaining patency of the venous system after intervention, and therefore, directly accessing the clot is not recommended and should be avoided whenever possible. One consideration when accessing below the knee is the length of catheters (diagnostic and infusion) and stents required to treat thrombus that may extend into the IVC.

Use of the smallest sheath size possible is suggested to minimize access site complications (typically 7–9 F), although 10- to 11-F sheaths may be required for placing larger stents.

5. Use of Intravascular Ultrasound

Intravascular ultrasound (IVUS) allows for detailed intraluminal assessment and can provide information on vessel diameter, venous wall irregularities, and hemodynamically significant (> 50%) stenoses in the venous system, which are often not appreciated on CT or venography. In addition, venous pressure gradients are notoriously inaccurate and often do not provide adequate information about the significance of venous stenoses. IVUS has been shown to be superior to single-plane venography in its estimation of degree of stenoses.[33] It can also be used to assess external compression, intravascular synechiae, collateral veins, and residual thrombus resistant to lysis. IVUS also has utility in stent deployment by showing its relative position as well as if the stent has completely conformed to the venous wall. In unilateral iliac stenosis (eg, May-Thurner syndrome), IVUS is extremely valuable in stent placement at or near the IVC origin (Figure 3).

6. Limited Use of IVC Filters

The risk of clinical PE in patients during catheter-based thrombus removal is not significantly increased compared to those on standard anticoagulation.[32] A

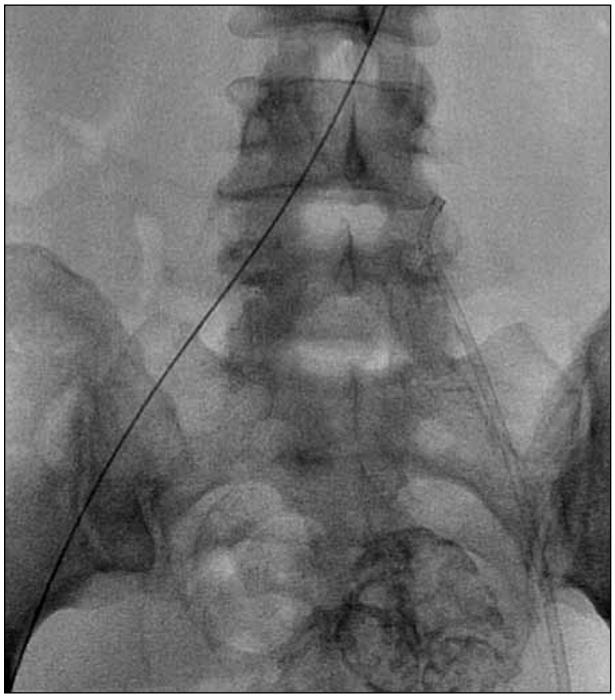

Figure 4. An 8-F guiding catheter (Vista Brite Tip, Cordis Corporation, Bridgewater, NJ) showing good wall apposition in the proximal left iliac vein during thrombus aspiration.

prospective study comparing permanent filters versus standard anticoagulation alone in patients with proximal DVT demonstrated an increased risk of recurrent DVT in the filter group with no survival benefit.[34] For this reason, temporary IVC filter placement before catheter-directed therapy is generally reserved for patients with a high risk for thrombus embolization, such as those with free-floating proximal thrombus that extends into the IVC. IVC filters are likely overused

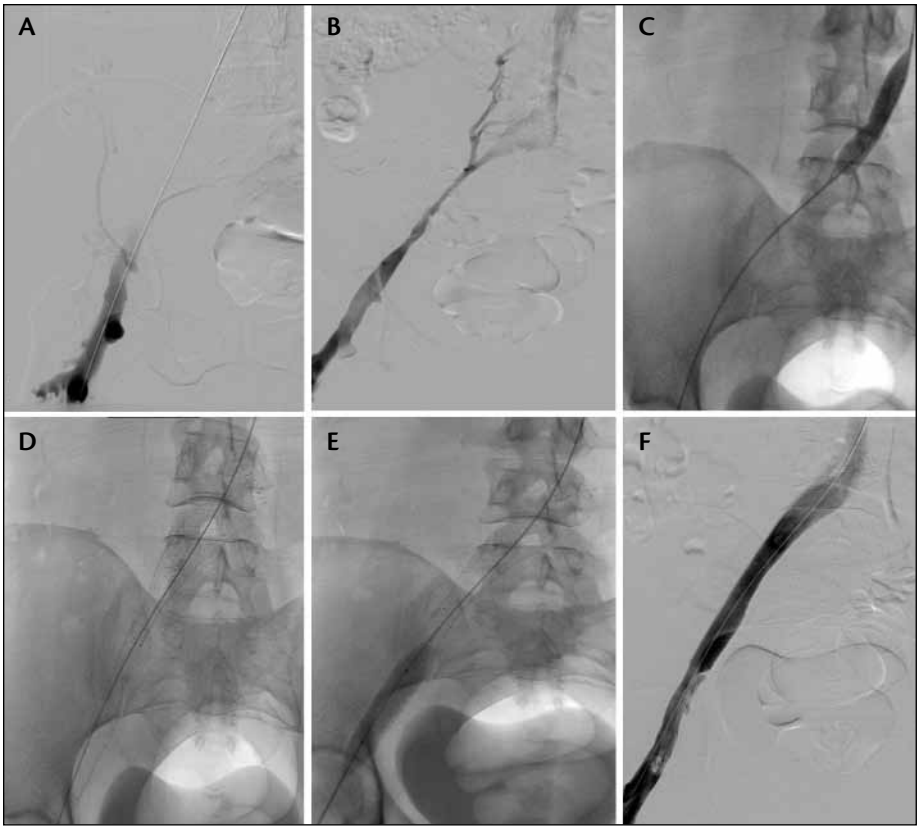

Figure 5. Venograms showing marked narrowing and filling defects of the left iliac vein (A, B), compatible with May-Thurner syndrome. After thrombectomy and venoplasty (C), stents are placed over the lesion using IVUS guidance (D). After balloon dilatation (E), final venography demonstrates patency (F).

for PDCT, and their use should be limited to specific situations. If a filter is placed during PCDT, the interventionist must be diligent in follow-up and attempt to schedule retrieval when clinically appropriate.

7. "Lyse and Wait" During Power Pulse Spray

Current pulsed-spray PCDT protocols have evolved over time to efficiently break down thrombus while minimizing the risk of adverse events such as bleeding. Initial enhancements to PCDT techniques were reported in acutely thrombosed hemodialysis grafts.[35-37] The "lyse-and-wait" technique was first described by Cynamon et al in a study of 18 occluded grafts that were injected with a thrombolytic agent at least 30 minutes before thrombectomy; compete clot lysis was achieved in all cases.[37] The currently accepted practice for PCDT is to allow the lytic agent to bathe and soften the clot for 20 to 45 minutes before thrombectomy.[20,24] The Power Pulse technique is a modification of the lyse-and-wait technique for use with the AngioJet catheter.

8. Use a Shaped Guide Catheter to Direct the AngioJet Catheter to Optimize Wall Apposition in the Iliac Veins and IVC

During lysis and thrombus aspiration, the AngioJet catheter can be maneuvered in a spiral fashion with the aid of a shaped guide catheter. We recommend using a curved 8-F guide catheter (cobra/hockeystick/multipurpose) to improve wall apposition (Figure 4).

9. Use Pneumatic Compression Devices to Improve Inflow During and After PCDT

Intermittent pneumatic compression (IPC) devices have established antithrombotic activity, preventing venous stasis by augmenting blood flow in the deep veins as well as increasing endogenous fibrinolytic activity by reducing plasminogen activator inhibitor-1.[38,39] One CDT study documented improved initial complete lysis, long-term patency, and valve function in patients who wore IPC devices.[40] In light of the current data and minimal adverse risks, we recommend IPC device use during and after PCDT. All patients receiving PCDT should go home with elastic compression stockings to be worn daily.

10. Judicious Use of Stents

Stenting after PCDT should be considered in the setting of structural lesions, which are often unmasked after clot lysis (eg, May-Thurner syndrome, pelvic sidewall tumor compressing the iliac vein) (Figure 5). Guidelines proposed by Vedantham et al recommend judicious use of stenting in more central disease (iliocaval) involving segments < 10 cm and, when possible, avoidance of stenting the common femoral vein across the femoral head.[27] Venous stents placed across the hip joint may be more prone to fracture and can eliminate a potential emergency venous access. IVUS may ultimately play a role in determining which stenoses are most in need of stenting, although further study is needed. The results of

the CAVENT trial suggest that failure to stent proximal lesions can lead to unacceptably high levels of PTS in patients after CDT.[41]

CONCLUSION

DVT affects a significant proportion of the population, many of whom go on to develop PTS. Rapid thrombus removal aims to preserve venous function and reduce the incidence of PTS. This has resulted in an emerging role for interventionists in the acute management of DVT. Successful outcomes depend on identifying appropriate candidates for therapy as well as understanding the current approaches, techniques, and equipment. ■

Vinit B. Amin, MD, is a resident physician in the Department of Radiology, Icahn School of Medicine at Mount Sinai in New York, New York. He stated that he has no disclosures related to this article. Dr. Amin may be reached at (212) 241-7409; vinit.amin@mountsinai.org.

Robert H. Siegelbaum, MD, is an Assistant Attending Radiologist, Interventional Radiology Service, Memorial Sloan-Kettering Cancer Center, and Assistant Professor of Radiology, Weill Cornell Medical College. He stated that he has no disclosures related to this article. Dr. Siegelbaum may be reached at (212) 639-2000.

Aaron M. Fischman, MD, is Assistant Professor of Radiology and Surgery, Division of Interventional Radiology, Icahn School of Medicine at Mount Sinai in New York, New York. He has disclosed that he is a consultant to Terumo Interventional Systems, Surefire Medical, and Celonova Biosciences. Dr. Fischman may be reached at (212) 241-7409; aaron.fischman@mountsinai.org.

Robert A. Lookstein, MD, is Chief of Interventional Radiology and Associate Professor of Radiology and Surgery, Division of Interventional Radiology, Icahn School of Medicine at Mount Sinai in New York, New York. He has disclosed that he serves as a consultant to Cordis and Bayer Healthcare. Dr. Lookstein may be reached at (212) 241-7409; robert.lookstein@mountsinai.org.

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