Produced under an educational grant from Possis Medical Inc. and Cordis Endovascular.

Aggressive DVT Management Strategies and Techniques

Experts share their experiences with early intervention using pharmacomechanical thrombectomy and temporary filter placement, which have shown rapid symptom resolution and encouraging outcomes.

At the annual Vascular Interventional Advances (VIVA) meeting in September 2007, Possis Medical Inc. (Minneapolis, MN) and Cordis Endovascular (a Johnson & Johnson company, Warren, NJ) held a symposium highlighting emerging trends in the treatment of deep vein thrombosis (DVT). Drs. Mark W. Mewissen, Anthony C. Venbrux, and Peter H. Lin were invited to discuss the incidence and nature of DVT and their experiences in treating this challenging patient population using today's techniques and technologies. This insert to *Endovascular Today* is a summary of the presentations given at VIVA '07 and the discussion shared by the panel.

PANEL MEMBERS

Mark W. Mewissen, MD, is Director of the Vascular Center at St. Luke's Medical Center in Milwaukee, Wisconsin. He has disclosed that he is a Vascular Advisory Board member for and has received honoraria from Boston Scientific Corporation, Cordis Endovascular, and Gore & Associates. Dr. Mewissen may be reached at (414) 385-2429; mark.mewissen@aurora.org.

Anthony C. Venbrux, MD, is Professor of Radiology and Surgery and Director of Cardiovascular and Interventional Radiology at The George Washington University Medical Center in Washington, DC. He has disclosed that he has received honoraria from Cook Medical, Cordis Endovascular, Bard Peripheral Vascular, Terumo Interventional Systems, Boston Scientific Corporation, and Rex Medical. Dr. Venbrux may be reached at (202) 715-5155; avenbrux@mfa.gwu.edu.

Peter H. Lin, MD, is Associate Professor of Surgery and Chief of the Division of Vascular Surgery & Endovascular Therapy, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, in Houston, Texas. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Lin may be reached at (713) 798-2151; plin@bcm.edu.

A NEW PARADIGM IN DVT MANAGEMENT

Presented by Mark W. Mewissen, MD

According to the 2004 ACCP Guidelines,[1] the standard of care for treatment of DVT is anticoagulation. These guidelines, which are scheduled to be revised in January 2008, include very little mention of thrombus removal as a strategy for DVT treatment. However, rapid thrombus removal in carefully selected patients using current catheter-directed and pharmacomechanical techniques have been demonstrated in the literature and are increasingly being used in today's practices.

GOALS OF DVT THERAPY

DVT of the lower extremity is recognized as a cause of both pulmonary embolism (PE) and the postthrombotic syndrome (PTS). Although anticoagulation is currently considered the standard of care for the prevention of PE and recurrent DVT, this form of therapy does not protect the patient from the manifestation of PTS, which can appear months to years after the acute episode of DVT.

Early thrombus removal is a logical approach to improve the long-term outcome of iliofemoral DVT. Today, natural history studies have shown that valve function is preserved with rapid physiologic lysis,[2] and clinical observations have indicated that valve function is preserved with successful lytic therapy.[3] Currently available interventional treatment

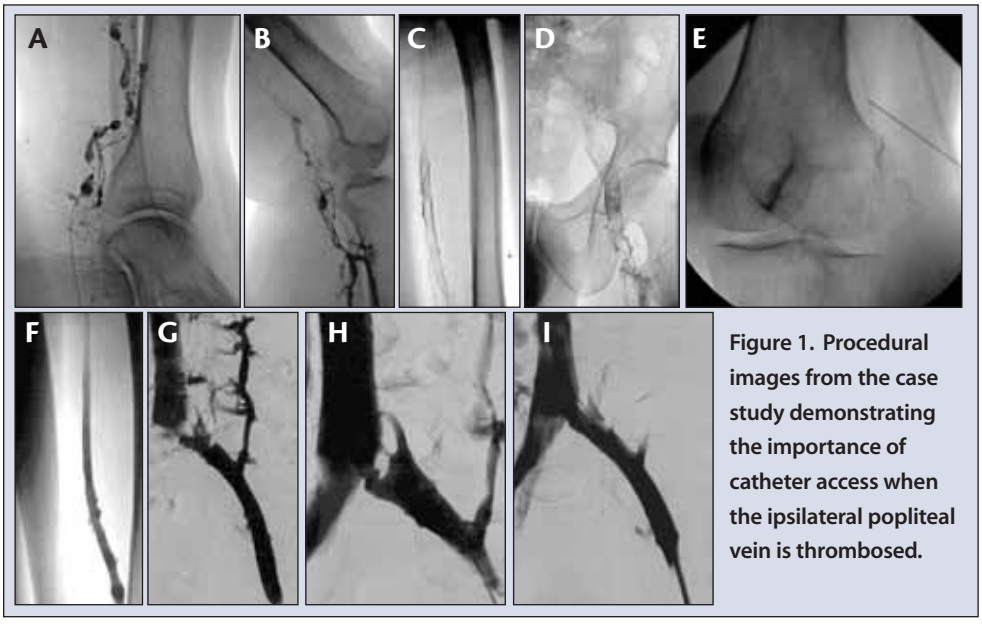

Figure 1. Procedural images from the case study demonstrating the importance of catheter access when the ipsilateral popliteal vein is thrombosed.

strategies include catheter-directed thrombolysis (CDT), pharmacomechanical thrombolysis (PMT), and, rarely, surgical thrombectomy. Strategies directed at early thrombus removal are attractive because they can help achieve restoration of the lumen and removal of the thrombus lining the venous valves. Two goals may be achieved: relief of venous outflow obstruction and preservation of valve function, both of which are established determinants of PTS.

Many patients with severe DVT, even when treated with anticoagulation, will still experience PTS. The first manifestations of PTS are pain and swelling of the lower extremity, and these symptoms are often observed in younger patients who are otherwise functional. In these patients, PTS treatment, which consists of compression stockings and leg elevation, is difficult due to their ambulatory needs. A recent study by Delis et al looked at the long-term effect of iliofemoral DVT on venous hemodynamics.[4] The investigators concluded that venous claudication occurs in almost 50% of patients with iliofemoral DVT, and it limits ambulation in close to 20%. There is marked hemodynamic impairment and significantly reduced quality of life, all related to PTS.

LESSONS FROM THE NATIONAL VENOUS REGISTRY

The DVT Lysis National Venous Registry, published in 1999, included 287 patients (303 limbs) treated at 63 academic and community centers.[5] Although it was a large registry that did not control for any inclusion variables, one of the goals was to gain an understanding as to which patients would likely benefit from aggressive therapy using catheter-directed lytic techniques. Overall, thrombosis-free survival was observed in 60% of patients at 12 months. There was a significant correlation of thrombosis-free survival with the results of initial therapy. Seventy-nine percent of those who had complete thrombus resolution had patent veins at 1 year, compared to 32% of those who had <50% of their thrombus dissolved. Notably, in a subgroup of acute, first-time iliofemoral DVT patients who had successful thrombolysis, 96% remained patent at 1 year. In addition to sustained patency, early success directly correlated with valve function at 6 months. Sixty-two percent of patients with <50% lysis had venous valvular incompetence, whereas 72% of patients who had complete lysis had normal valve function.

Although the registry constitutes a relatively low level of evidence-based medicine, it does indicate that there are patients who would clearly benefit from early thrombus removal using CDT or PMT. From these data, patients with acute iliofemoral DVT of less than 2 weeks' duration are very likely to benefit from a strategy directed at early thrombus removal.

CDT TECHNIQUES

The access technique we employ for CDT for patients with symptomatic iliofemoral DVT depends on whether there is popliteal vein thrombus involvement. If the popliteal vein is thrombosed, we gain access into the posterior tibial vein and also into the thrombosed popliteal vein in order to have two long-infusion catheters in place because we know that it is important to have the entire thrombus load impregnated with lytic agent. If the popliteal vein is not thrombosed, a popliteal stick under ultrasound guidance with the patient prone can be performed with relative ease.

Our technique is demonstrated in the following case study (Figure 1). A 45-year-old man presented with a 1-week history of worsening pain and swelling of the left lower extremity. Duplex study revealed DVT extending from the popliteal vein to the common iliac vein. After catheterization of the left posterior tibial vein at the ankle

under ultrasound guidance (Figure 1A), the noninvasive studies were confirmed at venography: There is thrombosis of the popliteal vein (Figure 1B), superficial femoral vein (Figure 1C), common femoral vein, and the external and common iliac veins (Figure 1D). After placement of a multisidehole catheter via the posterior tibial vein, the thrombosed left popliteal vein was catheterized via direct fluoroscopy access (Figure 1E), to place a second infusion catheter, therefore permeating the total thrombus length via two overlapping infusing catheters. After administration of 4.8 million units of urokinase at a rate of 200,000 units per hour, evenly split between the two catheters, complete lysis was demonstrated in all previously thrombosed veins (Figure 1F, G). The uncovered stenosis in the proximal common iliac vein (Figure 1H) was successfully treated with a self-expanding stent (Figure 1I). At 6-month follow-up, the deep veins remain patent, and the patient is asymptomatic.

This case is presented to highlight the importance of catheter access when the ipsilateral popliteal vein is thrombosed. To ensure that the entire thrombus burden is permeated with urokinase, the posterior tibial vein is punctured directly under ultrasound guidance. Via a 6-F sheath, a long, 5-F multisidehole catheter is then advanced to infuse the most proximal thrombus, usually at the level of the tibioperoneal venous trunk. The patient is then turned prone on the angiographic table to puncture the thrombosed popliteal vein. This can be performed with ultrasound guidance or by directly aiming the micropuncture needle at the 5-F infusing catheter inserted via the tibial vein. This "dual" tibial-popliteal venous access technique will allow the entire thrombus length to be infused, from the infrapopliteal veins to the inferior vena cava, if indicated.

Should extensive DVT be present with a patent popliteal vein, a "dual" popliteal access can easily be performed, accessing the popliteal vein with two sheaths and therefore allowing placement of overlapping long infusing catheters.

There are many unanswered questions related to CDT, including which lytic agent works best, as well as the ideal dosage and infusion rate and the role of heparin and GP IIb/IIIa inhibitors. We must also determine what it will take for the paradigm of DVT therapy to shift to an "intervention-first" approach, and exactly which patients and anatomical characteristics are most likely to be suitable for intervention. The ideal uses of mechanical thrombectomy devices and retrievable vena cava filters are also areas of continuing study. However, as we continue to see favorable results with increasing clinical experience, efforts must be made to help referring physicians become more aware of these emerging treatment options.

PREVENTING EMBOLIC COMPLICATIONS OF DVT

Presented by Anthony C. Venbrux, MD

In addition to chronic venous stasis ulcers and PTS, one of the most significant considerations in DVT patients is the risk of embolic complications, most notably PE. An estimated 140,000 to 200,000 people die in the US each year due to PE. If untreated, the mortality rate of PE is approximately 30%; however, if treated with anticoagulation therapy, this number can fall to 8%.

As detailed by Dr. Mewissen, an aggressive approach to DVT therapy using CDT or PMT clot lysis and removal can reduce thrombus-related complications in carefully selected patients. As an adjunct to this therapeutic option, many centers have begun placing vena cava filters to prevent dislodged debris from embolizing both peri- and postprocedurally. The concept of using a tethered filter to protect against venous thromboembolic disease was first published in 1968,[6] but the technology has come a long way since that time, with several removable filters having undergone clinical trials and receiving FDA approval.

In patients in whom filters have been placed, the reported incidences of caval thrombosis vary from as low as 3% to as high as 40% of patients. The reason for this wide discrepancy is the relative lack of data available for these patients, as well as the nature of the data that are available. Many of the published series include all comers, and the patients are not stratified according to their thrombotic risk. The nature of thromboembolic disease likely varies considerably across the numerous types of patients it can

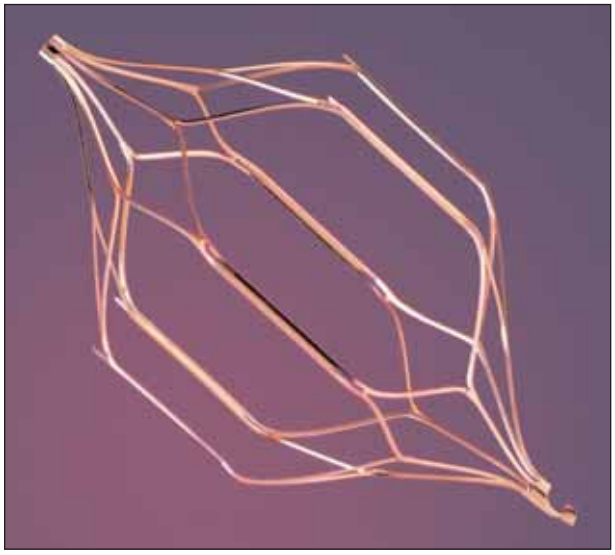

Figure 2. The OptEase retrievable filter (Cordis Endovascular, a Johnson & Johnson company, Warren, NJ).

affect, such as young trauma patients and patients with inherited defects, protein deficiencies, malignancies, etc.

THE WINDOW OF VULNERABILITY

In 1998, Decousus et al published a prospective, nonrandomized study showing a definite trend suggesting that the risk-benefit ratio associated with using vena cava filters changes over time.[7] In the acute setting of the first 12 days after placement, there was no question that filters saved lives. But at 2 years, patients with filters in place were experiencing an increased rate of thromboembolic events, such as PE and recurrent DVT. The idea that permanent filter placement could be associated with increased thromboembolic risk led to the development of retrievable filters, which are indicated for use in any patient at temporary risk for PE; in other words, these devices are designed to provide protection during a "window of vulnerability."

When optional filters became available and permanent placement was no longer necessary, we lowered our threshold for the application of filter use. The indications for placement of an optional filter are the same as those for a permanent filter. These include trauma, orthopedic, neurosurgical, bariatric and general surgery, GYN, oncology, and hematology patients, as well as patients with inferior vena cava or iliofemoral thrombus undergoing pharmacomechanical clot removal.

Four optional vena cava filters are available (although some are FDA approved only for permanent placement): Günther Tulip and Celect (Cook Medical, Bloomington, IN), OptEase (Cordis Endovascular, Warren, NJ), and Recovery/G2 (Bard Peripheral Vascular, Tempe, AZ); of these, the Günther Tulip and OptEase are FDA approved for optional (permanent or retrievable) placement.

The Günther Tulip is placed from a jugular or femoral approach, and it must be retrieved only from a jugular or upper-body approach. This retrieval can be done using a standard snare. The Celect filter is the next generation of the Günther Tulip, with the closed loops having been removed from the latter device, allowing it to be implanted for a longer period of time. The OptEase filter (Figure 2) can be placed using a small, 6-F deployment system, with separate kits available for both jugular/femoral and basilic vein approaches. The OptEase is the only optional filter that may be placed into a vena cava up to 30 mm, and it is also the only one that can be retrieved from a femoral approach using a standard snare. Significantly modified from the previous-generation Recovery filter, the G2 is a bilevel device available for use in up to 28-mm caval diameters. It requires a device-specific retrieval cone; standard snares should not be used.

In a patient who has a history of DVT and/or PE, an optional filter should only be removed after confirmation by imaging that a large thrombus is not trapped in the filter and a lower-extremity duplex ultrasound is negative. Anticoagulation therapy need not be reversed while the filter is in place.

The key to successful treatment of venous thromboembolic disease is to have a firm understanding of all of the therapeutic options available for each unique patient. Aggressive treatment and urgent referral are essential to reduce morbidity and mortality. In our experience, catheter-directed therapies may serve to maintain valve function, unmask underlying pathologies, and set the stage for further interventions. The use of vena cava filters may play a significant role in the treatment of this disease by protecting patients from devastating embolic complications, most notably PE.

MECHANICAL THROMBECTOMY TECHNIQUES

Presented by Peter H. Lin, MD

In treating patients who have acute DVT, there are numerous options available to the interventionist, including medical management, catheter-directed lysis, and a variety of interventional techniques. The appropriate treatment choice should be based on the specific symptoms and anatomy of the individual patient, as well as the associated risk-factor assessment.

EVALUATING TREATMENT OPTIONS

Prior to the era of endovascular interventions, acute symptomatic iliofemoral DVT was historically treated with a surgical approach. In the interest of complete discussion, the surgical option with balloon thrombectomy followed by femoral arteriovenous fistula creation should be mentioned, although for the most part, surgical removal is currently seldom used for acute DVT patients. For the majority of patients who present with iliofemoral DVT, outpatient anticoagulation using low-molecular-weight heparin is the most commonly administered therapy, particularly if the patient has only mild symptoms and is likely to be compliant to therapy. However, if the patient has significant symptoms or fails to respond to outpatient anticoagulation therapy, it is often necessary to treat these patients in an inpatient setting using unfractionated heparin in an IV drip, followed by warfarin for anywhere from 3 to 6 months.

Anticoagulation with heparin or coumadin is very effective in preventing propagation of thrombus, but it does not remove the existing burden. As discussed previously, the possible dangers of PE and the discomforts of PTS may be significantly reduced if the clot burden is lysed and/or removed. Endovascular techniques such as CDT and PMT

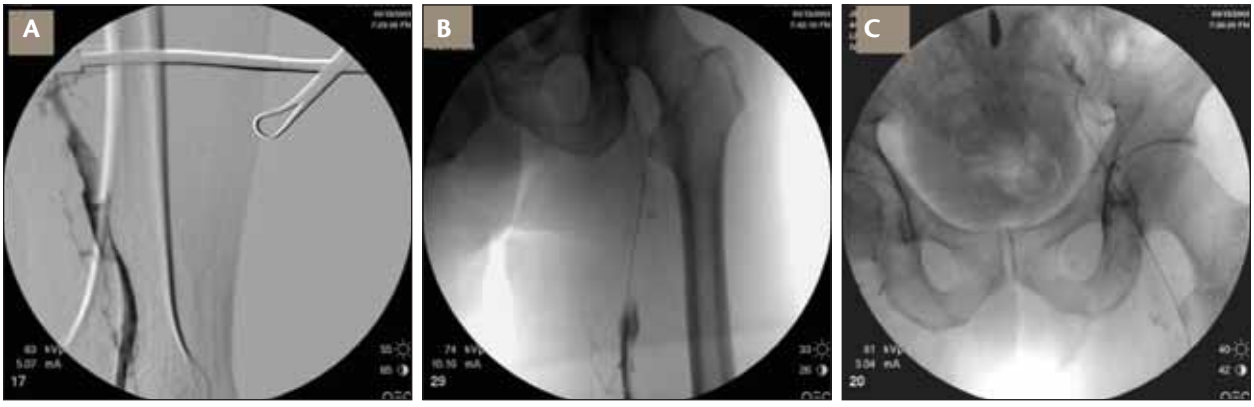

Figure 3. Initial venograms showing a large amount of thrombus in the superficial femoral vein (A), common femoral vein (B), and the iliac venous system (C).

have emerged as viable options for treating and removing thrombus burden in recent years as this technology has evolved. These techniques may also have the theoretical advantage of restoring valve function, thereby preventing subsequent valve dysfunction or PTS incidence.

CDT can be effective in dissolving thrombus and revealing the underlying lesion or stenosis, after which more direct treatment can be delivered (eg, angioplasty and stenting). Additionally, CDT allows the lytic agent to penetrate into the small surrounding vessels, which are otherwise inaccessible with balloon catheters and other devices. However, this technique does have some limitations. First, the patient must be kept in the ICU with a continuous IV drip. Also, if a catheter has been placed in the groin, the patient must be kept on complete bed rest. Serial blood tests must also be monitored to ensure the fibrinogen level and other serum markers such as platelets, PT, and PTT remain stable. These serum blood evaluations are typically performed every 8 hours for as long as CDT is administered. Prolonged duration of CDT can also lead to bleeding complications, and all of these factors require extensive nursing care involvement.

PMT AND THE POWER-PULSE SPRAY TECHNIQUE

Our institutional preference for managing symptomatic acute DVT patients is the Power-Pulse Spray technique using the AngioJet® Rheolytic™ Thrombectomy System (Possis Medical, Inc., Minneapolis, MN). The Power-Pulse Spray technique encompasses the use of two treatment modalities: Power-Pulsed thrombolytic agent delivery and mechanical thrombectomy. We also consider using retrievable vena cava filters on an individual patient basis depending on symptoms and thrombus burden. We use tPA as our lytic agent.

Our technique can be illustrated in the following case. After a 12-hour trans-Atlantic flight from Paris to Houston, the patient presented to the ER with swelling of the right leg after 3 days. Ultrasound in the ER showed a large thrombus in the iliofemoral system. Based on this diagnosis and the patient's symptoms, which included leg swelling, severe pain, and inability to bear his body weight on his leg, our treatment plan was as follows. First, we placed a retrievable filter via left groin access with the patient in a supine position. For this particular indication, our filter of choice is the OptEase because this device can be retrieved from the groin approach, rather than the jugular. This is especially helpful if a stenting procedure is part of the therapy, after which the filter can be retrieved from the same access point if it is determined to be free of any thrombus. For this particular indication, we believe that groin retrieval also provides short-term advantages from a patient-comfort standpoint.

Once the filter was placed, the patient was turned to a prone position, and his right popliteal vein was accessed using ultrasound guidance. Using a portable ultrasound unit, the occluded vein can be accessed very easily with a .014-inch guidewire. Once this was achieved, the guidewire was exchanged for a .035-inch guidewire, the dilator was removed, and the initial venogram was performed (Figure 3). In this patient, a large amount of thrombus was discovered in the superficial femoral vein, common femoral vein, and iliac venous system. The clot was then treated with PMT using the Power-Pulse Spray technique, in which thrombolytic agent was mechanically delivered directly into the thrombus, which was followed by a "lysis-and-wait" period of approximately 15 minutes. During this period, thrombolytic agent was allowed to exert its pharmacologic effect by breaking down the venous thrombus. The Power-Pulse Spray technique was completed with mechanical thrombectomy in which the AngioJet catheter was activated to remove all remaining venous thrombus.

Possis recently introduced the newest generation of the AngioJet system, which consists of a much smaller drive unit

Figure 4. The AngioJet System pulls thrombus from the vessel into the catheter where it is fragmented and removed from the body.

that performs the same clinical function. Once this catheter system is activated, seven high-velocity jet streams are emitted in a coaxial wave. By placing this catheter in an enclosed space, the activation of this high-velocity jet stream will create an absolute vacuum, known as the Venturi effect. The suction created is the means by which the AngioJet removes thrombus (Figure 4).

The AngioJet system can be used in both normal thrombectomy and Power-Pulse Spray modes. To perform Power-Pulse Spray, a specific kit is connected to the system, allowing two solution bags to be hung and the physician to connect saline and a small IV bag containing a lytic agent to separate ports. We use 10 mg of lytic agent in a 50-mL solution.

Using the AngioJet Power-Pulse mode, the outflow is blocked, making the AngioJet catheter into a power-infusion system. With the Gen II system, a stopcock is placed on the outflow lumen to occlude the flow. When the outflow channel is blocked, the lytic agent is forcefully delivered into the thrombus itself. However, with the newer-generation AngioJet Ultra console, which became available in 2007, when a catheter is connected to the drive unit, the system will ask if the physician wants to use Power-Pulse Spray. If the answer is yes, the outflow channel of the catheter will automatically be shut off; manipulation of the three-way stopcock is not necessary with the new system.

We allow the medication to infuse the thrombus for approximately 15 to 20 minutes. A venogram taken at this point in this patient shows that there is improvement, but that significant thrombus remains (Figure 5). Next, the thrombectomy mode of the AngioJet was activated by opening the outflow channel, and the residual thrombus was removed, which was confirmed by venogram (Figure 6). We successfully identified the lesion, which was treated with angioplasty and stenting. Returning our attention to the vena cava, we saw that there was significant thrombus trapped in the OptEase filter over the 2-hour duration of the procedure. Although one can theoretically remove the thrombus trapped within the IVC filter, it is not our routine practice to perform thrombectomy for thrombus trapped inside the filter, because we believe these thrombi would be dissolved by spontaneous thrombolysis. We typically leave the IVC filter in place and initiate systemic anticoagulation therapy with IV heparin followed by oral coumadin. Pre- and 2-day postprocedure photographs show the dramatic improvement in this patient after aggressive DVT therapy (Figure 7).

Because there was thrombus found in the filter, we left it in place and brought the patient back several weeks later for evaluation. After 3 weeks, the patient returned, and ultrasound examination showed no thrombus in the filter. We then gained access via the groin and obtained a venogram confirming that no thrombus remained. To remove the filter, we used a standard snare (EN Snare; InterV, Dartmouth, MA). By drawing the snare under the filter, we were able to easily engage one of the loops of the snare onto the hook on the lower portion of the filter. The next step was to slowly provide gentle downward traction; the filter was kept in traction with the snare and captured inside the sheath by advancing the sheath forward. The device was then removed in its entirety. A completion venogram showed that there was no residual thrombus and that the filter removal was successful.

CDT AND PMT: A HEAD-TO-HEAD EVALUATION

Our institution conducted an 8-year retrospective study comparing CDT to PMT in patients with symptomatic DVT, analyzing both treatment outcomes and cost-effectiveness.[8]

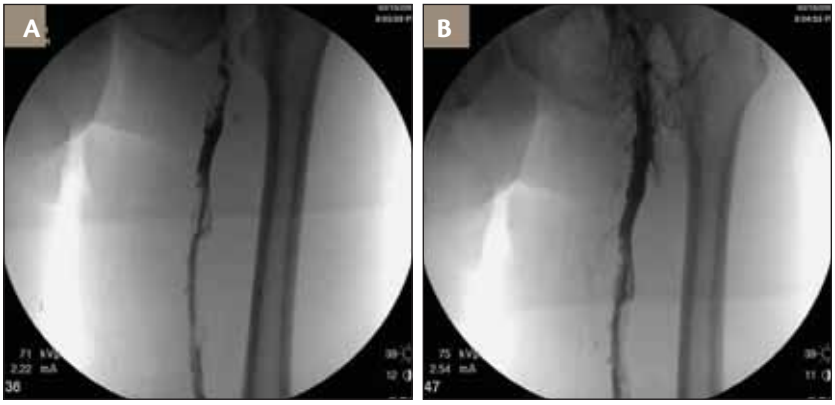

Figure 5. A venogram taken after lytic infusion shows that there is improvement, but that significant thrombus remains.

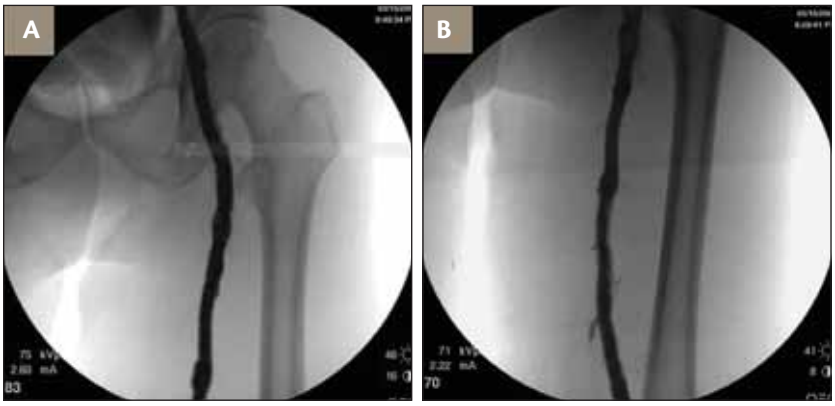

Figure 6. Venograms confirming removal of residual thrombus using mechanical thrombectomy.

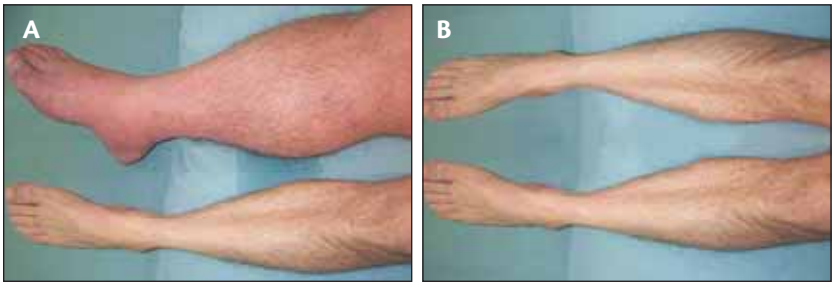

Figure 7. Pre- and 2-day postprocedure photographs show the dramatic improvement in this patient after aggressive DVT therapy.

The patients were treated during the same time period, and both cohorts were relatively similar in demographics. The average age of the thrombus in both groups was approximately 2 weeks from the onset of symptoms. The treatment outcomes in each group showed remarkable therapeutic success in terms of both radiographic appearance and clinical response, with no statistically significant difference between the two cohorts. The majority of patients in both groups underwent adjuvant angioplasty or stenting. One area where the groups differed was that significantly fewer venograms were required in the PMT group (0.4±0.2) as compared to the CDT group (2.5±0.7). The PMT group also saw reductions versus the CDT group in duration of treatment (76±34 min vs 1.8±0.8 days); mean ICU stay (0.6±0.3 days vs 2.4±1.2 days); overall length of hospital stay (4.6±1.3 days vs 8.4±2.3 days); and red blood cell transfusion (0.2±0.3 units vs 1.2±0.7 units).

In terms of the cost analysis, the PMT patients were treated in the OR, whereas the CDT patients underwent therapy in the radiology suite; consequently, a direct cost comparison in this regard is not feasible, but it should be noted that the costs related to the OR are higher. However, due in large part to the reduction in ICU and overall length of stay, there is a significant reduction in the total cost of PMT therapy ($47,742±$19,247) compared to CDT ($85,301±$24,832). Additionally, in our current practice, many of these PMT procedures now take place in the cath lab or radiology suite, with lower associated costs than indicated in our study.

In summary, the significant finding of the study is that patients undergoing PMT will have significantly reduced numbers of venograms required, ICU stay, hospital stay, and red blood cell transfusion requirements than those undergoing CDT. The hospital costs associated with PMT were found to be half those of CDT therapy. Both therapeutic options were found to be equally efficacious in terms of clinical response and radiographic outcome in patients with acute DVT.

CONCLUDING REMARKS

New options are emerging for the treatment of DVT patients. These techniques and technologies go beyond the current standard anticoagulation therapy, and early experiences have shown benefits such as immediate relief of symptoms, quicker recovery times, and earlier return to normal life in carefully selected patients. However, the belief that early and urgent removal of thrombus will reduce the incidence of PTS has not yet fully been proven, although limited data and clinical experiences indicate that valve function may be better preserved using this approach, decreasing the incidence of future PTS development. Further study evaluating the use of PMT alone and in conjunction with retrievable filters is needed to fully determine the extent of these possible benefits. ■

1. Buller HR, Agnelli GH, Hull RD et al. Antithrombotic therapy for venous thromboembolic disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(Suppl):401S-428S.
2. Meissner MH, Manzo RA, Bergelin RO, et al. Deep venous insufficiency: the relationship between lysis and subsequent reflux. 1993;18:596-605.
3. Jeffrey P. 2nd Int'l Vasc Symposium. London. 1986.
4. Delis KT, Bountouroglou D, Mansfield AO. Venous claudication in iliofemoral thrombosis: long-term effects on venous hemodynamics, clinical status, and quality of life. Ann Surg. 2004;239:118-126.
5. Mewissen MW, Seabrook GR, Meissner MH, et al. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. Radiology. 1999;211:39-49.
6. Eichelter P, Schenk WG Jr. Prophylaxis of pulmonary embolism: a new experimental approach with initial results. Arch Surg. 1968;97:348-356.
7. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena cava filters in the prevention of pulmonary embolism in patients with proximal deep vein thrombosis. N Engl J Med. 1998;338:409-415.
8. Lin PH, Zhou W, Dardik A, et al. Catheter-direct thrombolysis versus pharmacomechanical thrombectomy for treatment of symptomatic lower extremity deep venous thrombosis. 2006;192:782-788.