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EVOLVING DVT TREATMENT

and the Patient Care Continuum

Leading experts discuss where we are today, where we need to go, and utilizing a team-based approach to get there.

EVOLVING DVT TREATMENT

and the Patient Care Continuum

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The ABCs of Iliofemoral DVT

Understanding the continuum of care through a team-based approach.

BY DAVID M. LIU, MD, FRCPC, FSIR; BEHRANG HOMAYOON, MD, FRCPC; AND JOHN CHUNG, MD, FRCPC

A 22-year-old athlete with a history of the factor V Leiden mutation and previous deep vein thrombosis (DVT) presented to his primary care physician with a swollen right leg after running a race over the weekend in hot weather. A 46-year-old woman bound to a wheelchair who had stage IV ovarian cancer developed progressive bilateral lower extremity leg swelling that had become intolerable and a remote history of an inferior vena cava (IVC) filter placed. A 32-year-old woman with intrauterine fetal demise underwent therapeutic abortion with a dose of mifepristone. A 50-year-old man with recent air travel history experienced sudden increased swelling and erythema of the right thigh to the ankle. These patients have a suspicion of iliofemoral DVT and present with different prodromes, circumstances, and needs in the management of their suspected DVT. The intent of this article is to provide a general outline and flow, taking into consideration the continuum of care in a multidisciplinary hospital-based model utilizing the recently published *Interdisciplinary Expert Panel on Iliofemoral DVT* (*InterEPID*) as the basis for discussion (Figure 1).[1]

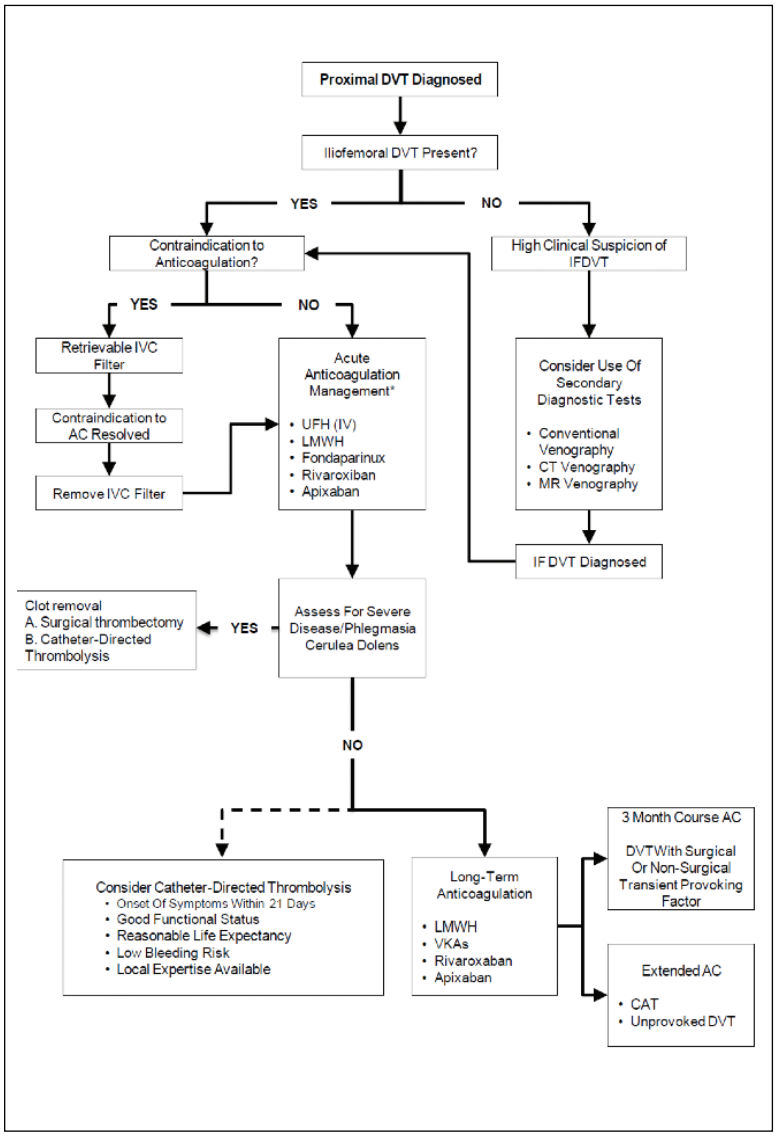

Figure 1. Multidisciplinary decision tree-based approach to the diagnosis and management of IF-DVT. In the absence of severe symptoms, catheter-directed thrombolysis may be considered in select patients with iliofemoral DVT (dotted line). Abbreviations: AC, anticoagulation; CAT, cancer-associated thrombosis; IF-DVT, iliofemoral DVT; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VKAs, vitamin K antagonists. Reproduced with permission from CMAJ. 2015;187:1288–1296.

INTAKE AND DIAGNOSIS

Early clinical suspicion and initiation of appropriate workup is key to improving overall outcomes of lower extremity DVT. There are no symptoms specific to lower extremity DVT; however, lower extremity swelling, pain, and warmth are common.[2] Risk factor assessment and a thorough history eliciting the timing and onset of symptoms, baseline functional status, presence of underlying systemic disease, family history of venous

thromboembolism, and history of medications that may cause lower extremity edema is paramount at presentation. Postpartum state, recent lower extremity trauma, major surgery, and immobilization, among other factors, have been identified as major risk factors for the development of DVT and should be sought out at initial clinical assessment.[3]

On physical examination, it is important to assess the location and laterality of lower extremity edema and to characterize any associated skin changes or ulcerations. The presence of phlegmasia cerulean dolens, which includes the triad of edema, cyanosis, and pain and heralds underlying hypercoagulable state or malignancy, indicating the need for urgent treatment escalation beyond anticoagulation, must be excluded.[4]

The Wells score can be used in the decision-making process to establish the pretest probability of DVT. A large meta-analysis concluded that individual clinical features have a limited value in the diagnosis of DVT, and overall assessment of clinical probability using the Wells score is more useful. However, it has not been validated as a severity score and therefore cannot be utilized to differentiate patients that may potentially benefit from endovascular intervention or thrombolysis.[5] D-dimer has a limited value in the diagnostic algorithm, but has a very high negative predictive value in the setting of venous thromboembolism, and can be used if the pretest probability of DVT is low.[2]

An objective test, most commonly duplex venous sonography, is required to establish the diagnosis of lower extremity DVT. This can be supplemented with CT or magnetic resonance venography to better assess the IVC and iliac veins. If endovascular therapy is planned, CT or magnetic resonance venography may provide useful information that may alter the therapeutic approach, such as the site of venous access and thrombus removal methods. Further imaging such as echocardiography and lymphoscintigraphy and other laboratory tests (thyroid function, complete blood count, antinuclear antibody) play adjunct roles in select patients with lower extremity edema to assess for alternative diagnoses.

Thrombophilia testing can be initiated in select patients who are considered at high risk for having a hypercoagulable disorder but is not routinely offered to all patients with DVT because, in most patients with DVT, the identification of an inheritable defect does not alter the anticoagulation regimen.[6] Furthermore, studies have shown that the presence of single or multiple thrombophilic defects does not seem to be associated with a higher risk of recurrent venous thromboembolism.[7]

THERAPY OBJECTIVES

Each of the previous case examples is provided to emphasize the high degree of variability in presentation and the need to appreciate the context in which therapy is to be considered. In some cases, the acuity and/or severity of symptoms mandates urgent intervention. In other cases, where the onset is gradual and symptoms are less severe, practical application of the principle of the open vein hypothesis (to preserve or maintain normal venous hemodynamics and valvular function) may justify intervention.

Regardless of whether endovascular intervention is warranted, anticoagulation is the mainstay of therapy for patients with lower extremity DVT. All patients, with no contraindications, should be anticoagulated for a finite period following the first episode of lower extremity DVT, although some may benefit from indefinite anticoagulation to reduce the risk of recurrent thrombosis.[8] IVC filter placement is a consideration in appropriately selected patients. Furthermore, studies have shown early ambulation is not associated with progression of DVT or development of pulmonary embolism and should be encouraged.[9,10] At this point in time, anticoagulation is the only therapy that has demonstrated a decrease in mortality related to subsequent events, such as fatal pulmonary embolization.[11]

Despite optimal anticoagulation, > 30% of patients with a history of symptomatic DVT will develop symptomatic post-thrombotic syndrome (PTS), likely due to chronic venous occlusion, suboptimal collateralization pathways, and venous valvular dysfunction. Up to one-third of these patients will develop severe debilitating symptoms.[12] Based on generic and disease-specific quality-of-life measures, it is well established that PTS has a significant negative impact on a patient's quality of life.[13,14] Kahn et al have demonstrated that self-reported physical quality of life in patients with PTS is comparable to patients with other chronic illnesses such as diabetes, chronic obstructive lung disease, and congestive heart failure.[14] There is no convincing evidence that the use of graduated compression stockings in the setting of lower extremity DVT reduces the incidence of PTS with more recent definitive studies (such as the SOX randomized controlled trial) demonstrating no significant reduction in the incidence of PTS.[15,16] Furthermore, cost and lack of comfort reduce patient compliance.

Lack of endoluminal venous recanalization within the first 6 months after an acute lower extremity DVT has been shown to be an important predictor of PTS.[17] Based on similar observations, the open vein hypothesis

postulates that immediate and effective removal of acute venous thrombus will reduce the risk of PTS and thereby improve quality of life.[18]

The ATTRACT (Acute Venous Thrombosis: Thrombus Removal and Adjunctive Catheter-Directed Thrombolysis) randomized controlled trial is looking to demonstrate PTS incidence reduction.[19,20] The CaVenT trial, which randomized 209 patients with iliofemoral DVT to catheter-directed thrombolysis (CDT) plus anticoagulation or anticoagulation alone, showed that 43% of patients in the CDT arm developed PTS, while 71% of patients who underwent anticoagulation alone developed PTS, based on the Villalta score at 5 years. The difference in PTS between the two arms corresponded to an absolute risk reduction of 28% and a number needed to treat (NTT) of 4.[21] The study suggests that early clot removal, by means of absolute PTS risk reduction, may have a beneficial long-term effect and should be offered to appropriately selected patients. It may also be that "the low incidence of adjunctive venous stenting in the CaVenT trial may have diminished the overall benefit of CDT."[22]

Therefore, after a thorough workup, it may be appropriate to apply the open vein hypothesis, escalate therapy beyond standard anticoagulation, and offer endovascular options to appropriately selected patients. According to the 2016 American College of Chest Physicians guidelines, "patients who are most likely to benefit from CDT, who attach a high value to prevention of PTS, and a lower value to the initial complexity, cost, and risk of bleeding with CDT, are likely to choose CDT over anticoagulation alone."[23]

THE SYSTEM BEYOND THE PROCEDURE

The treatment of acute iliofemoral DVT does not begin and end in the angiography suite and requires a methodical approach to treatment. Due to the multitude of presentations, in addition to the many diagnostic and therapeutic pathways that exist in both outpatient and hospital-based practices, there is a need to identify all stakeholders and incorporate institutional knowledge and experience to develop system-wide protocols and evidence-based programs that provide common pathways from multiple intake sources.

The consideration of clot removal strategy (eg, surgery, mechanical, pharmacological) should only be made after appropriate diagnosis and a recognition of postprocedural care is determined. Rather than creating arbitrary criteria for intervention, decisions and options should be considered at the time of primary intake. Whether from the emergency room physician, hospitalist, or primary care provider, the appropriateness of consultation for further management relies on confirmation of diagnosis, urgency, and goals of therapy.

Patient management considerations, such as anticoagulation (heparin, vitamin K antagonists or direct oral anticoagulants), rehabilitation, follow-up imaging, and potential management of PTS should be recognized as part of the care continuum. Establishing response teams, core expertise, and executive decision guided by a treatment algorithm based on best evidence or local expertise provides clear management pathways (Figure 1).[1]

CONSIDERATIONS TO THERAPY

Patient Considerations

First and foremost, having an established acute iliofemoral DVT intake institutional protocol that directs patients presenting in different settings (inpatient, outpatient referral, emergency room) toward a common multidisciplinary assessment pathway (that may include interventional radiology, vascular surgery, and hematology) optimizes downstream decisions (Figure 1).[1]

A standardized assessment can then be performed, which could take into consideration numerous patient factors, including:

- *Acuity of thrombus/DVT symptoms.* It has been established that acuity of < 21 days benefits the most from an intervention. Beyond this time, retraction and solidification of thrombus limits the efficacy of chemical lysis.[1,21]
- *Type of patient.* A young, active patient is likely to suffer far more from PTS than a bedridden or wheelchair-bound patient who may already have very limited mobility at baseline. In the former, more aggressive thrombus clearance may be beneficial.[1,19,21]
- *Severity of symptoms.* In a patient with relatively mild symptoms, such as minor leg swelling and short-segment femoral-only DVT, medical management can be first-line treatment with early follow-up (at 2 weeks). This contrasts with severely symptomatic patients with phlegmasia and extensive occlusive iliofemoral DVT, in which case more aggressive thrombus clearance/lysis may be warranted for limb preservation.[1]
- *Temporal evolution of symptoms.* Patients who present with worsening symptoms after successful anticoagulation represent a population that may require further intervention. Clinical follow-up at 1 week after anticoagulation initiation may help identify this subpopulation.
- *Underlying contributions to acute DVT.* Primary or secondary pelvic neoplasia can physically compress pelvic veins and incite DVT formation. If the patient presents with unilateral left leg DVT, consideration for underlying May-Thurner syndrome should be made (extrinsic compression of the left common iliac vein with reac-

tive intimal hyperplasia due to an overlying right common iliac artery).

- *Contraindication to systemic anticoagulation.* If the patient is immediately postoperative from major neurological surgery, has suffered from an acute cerebral infarct, or has some other contraindication to systemic anticoagulation, consideration could be given to limited pharmacomechanical thrombectomy (PMT) or even solely mechanical thrombectomy in the first instance.

Procedural and Postprocedural Considerations

Assuming CDT or PMT therapy has been chosen, a range of currently available treatment devices exist. The most basic of these is CDT, in which an infusion catheter is placed across the acute thrombus, and slow, continuous infusion of a chemical thrombolysis agent is initiated. Newer devices combine some form of mechanical disruption of the thrombus in conjunction with chemical lysis. The two most widely used of these pharmacomechanical thrombolytic (PMT) devices are the AngioJet™ (Boston Scientific Corporation) and EKOS (BTG International) systems. Several alternative PMT devices have become available to the market, however, the aforementioned devices represent those with the longest history of safety and use.

A detailed discussion regarding techniques specific to the PMT devices is beyond the scope of this article. Briefly, however, AngioJet combines chemical thrombolysis via Power Pulse™ with rheolytic fluid-based disruption of thrombus and catheter-based aspiration thrombectomy.[24] EKOS combines chemical CDT with low-power, high-frequency ultrasound application to the proprietary infusion catheter/wire combination, with the ultrasonic vibration purported to hasten thrombus disruption.[25] There is evidence suggesting PMT quickens thrombolysis in the early setting compared with CDT alone.[24,25] The AngioJet Power Pulse technique is preferred in our institutions when approaching acute iliofemoral DVT with subsequent TPA infusion if required and reconstruction either via venoplasty and/or stent placement when maximum clot removal has been achieved.

The primary postprocedure consideration for CDT is the availability of continuous in-hospital monitoring for CDT patients to minimize and expedite early detection of CDT-related complications. In institutions where beds with continuous monitoring are limited or not available, PMT may be chosen over standard CDT to reduce the continuous monitoring requirements, sometimes as a single-session PMT without postprocedural continuous infusion CDT.[24]

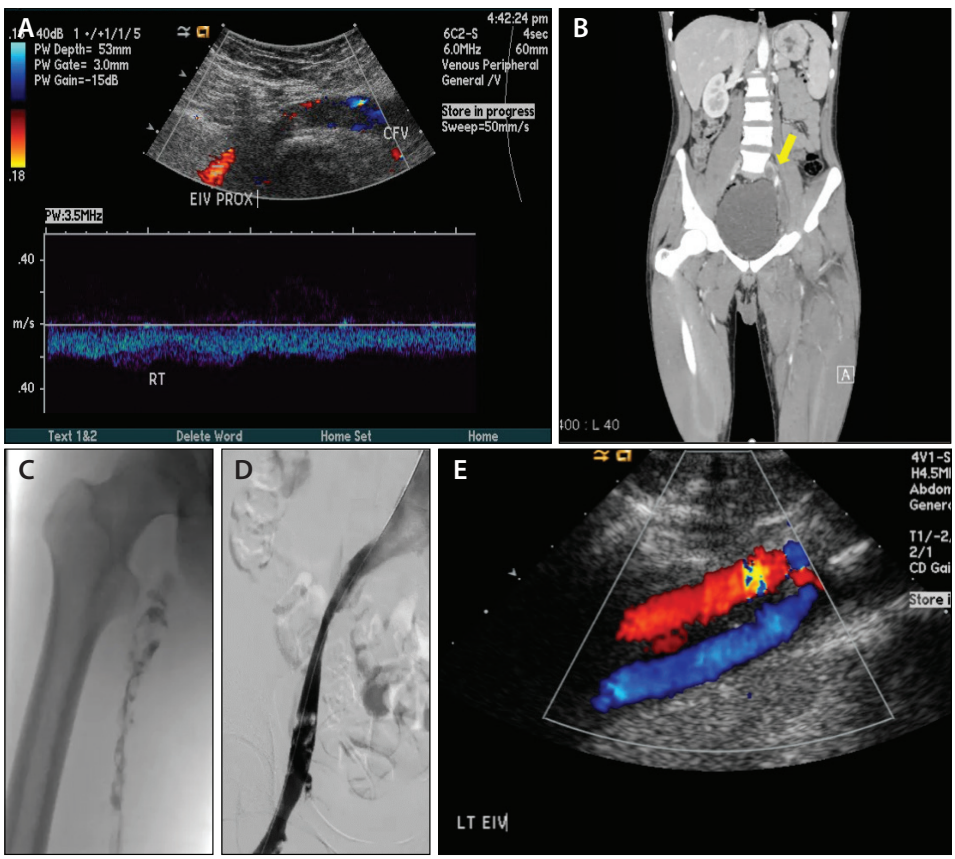

Figure 2. A 22-year-old athlete with factor V Leiden mutation and previous DVT. Ultrasound confirming external iliac DVT (A). CT confirming iliofemoral DVT (B). DSA angiogram demonstrating extensive clot in common femoral distribution (C). After AngioJet Power Pulse technique utilizing a Solent Omni catheter with 20 mg TPA and balloon venoplasty (D). Six-month follow-up ultrasound following anticoagulation with NOAC demonstrating patency, with return to baseline function (E).

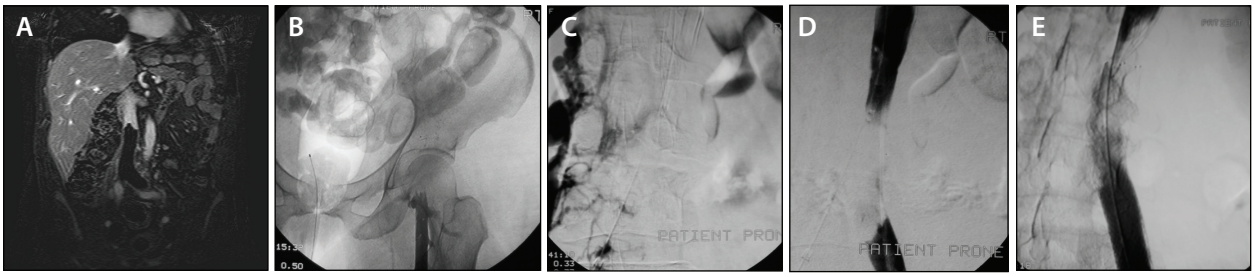

Figure 3. A 46-year-old woman with stage IV ovarian cancer and bilateral lower extremity swelling with IVC filter in place. Coronal contrast-enhanced MRI demonstrating extensive clot initiating from the IVC filter (A). Left popliteal venogram showing complete occlusion of the left superficial femoral vein (B). Right iliac venogram demonstrating extensive collateralization from the venous plexus and occlusion of the common iliac vein (C). After 24-hour TPA via catheter-based infusion, both legs reestablished flow in the left femoral and iliac systems with markedly reduced edema and persistent occlusion of the IVC from residual clot/tumor (D). Subsequent stenting returned inline flow (E) and alleviation of leg pain, edema, and swelling. The patient was placed on lifelong low-molecular-weight heparin and palliative care for 4 months prior to death.

Considerations and Case Examples

The 22-year-old male athlete presented with symptoms of acute DVT (Figure 2). Initial standardized intake assessment should be performed to substantiate a diagnosis of acute iliofemoral DVT. Given the patient's age, it would be reasonable to pursue CDT/PMT over standard anticoagulation to expedite thrombus clearance and minimize the propensity of PTS, especially if the DVT extends into the iliac veins.[1,19,21] Because he has an underlying coagulopathy and history of prior DVT, hematology assessment with consideration for long-term anticoagulation could be made.[1]

The middle-aged, wheelchair-bound woman with advanced-stage cancer and progressive, intolerable leg swelling is a much more complex case (Figure 3). To start, iliofemoral DVT should be established. More in-depth imaging is likely necessary to determine the extent of the pelvic cancer and the degree to which the neoplasia is contributing to venous occlusion either by vascular invasion or extrinsic compression. The end objective for this patient should also be clearly established to help determine the type of treatment to pursue. Treatment could range from conservative with pneumatic compression stockings with or without anticoagulation (and in the case of cancer-related thrombosis, be restricted to low-molecular-weight heparin) to palliative surgical debulking with thrombectomy.[1]

The 32-year old woman who was posttherapeutic abortion presented with bilateral DVT (Figure 4). As with the other cases, iliofemoral DVT should be substantiated. Given the patient's young age, it would be reasonable to pursue CDT/PMT over standard anticoagulation to expedite thrombus clearance and minimize the propensity of PTS (especially in iliofemoral DVT) given the potential greater long-term deleterious consequences of PTS in this patient population.[1,19,21]

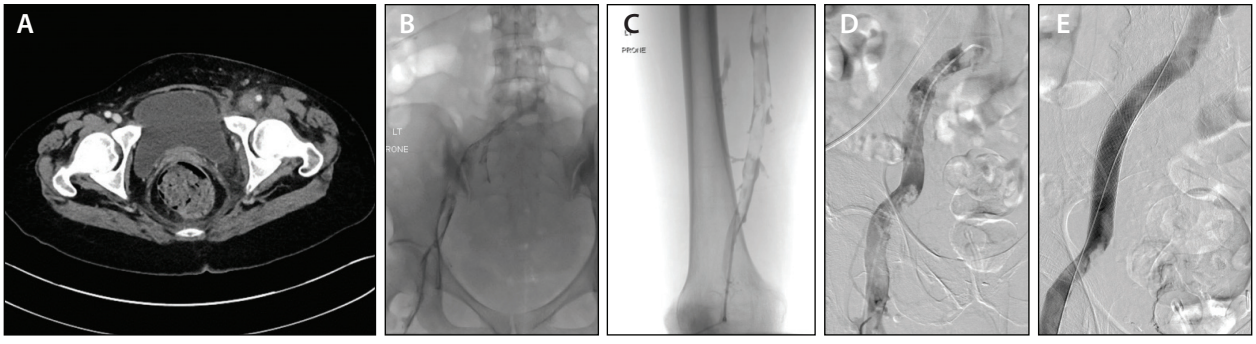

Figure 4. A 32-year-old postpartum woman with acute onset DVT. Pregnant with intrauterine fetal demise, she underwent therapeutic abortion with a dose of mifepristone. CT scan demonstrating left-sided common femoral DVT (with extension to common iliac vein not shown) (A). Injection venogram revealing extensive iliofemoral DVT (B,C). After AngioJet Power Pulse technique utilizing a ZelanteDVT catheter with 20 mg TPA, there was return of flow and persistent clot/stenosis in the left common iliac vein (May-Thurner syndrome) (D) with subsequent stenting (Innova [Boston Scientific Corporation], 12 X 80 mm) (E). She was placed on warfarin for 6 months with return to baseline function.

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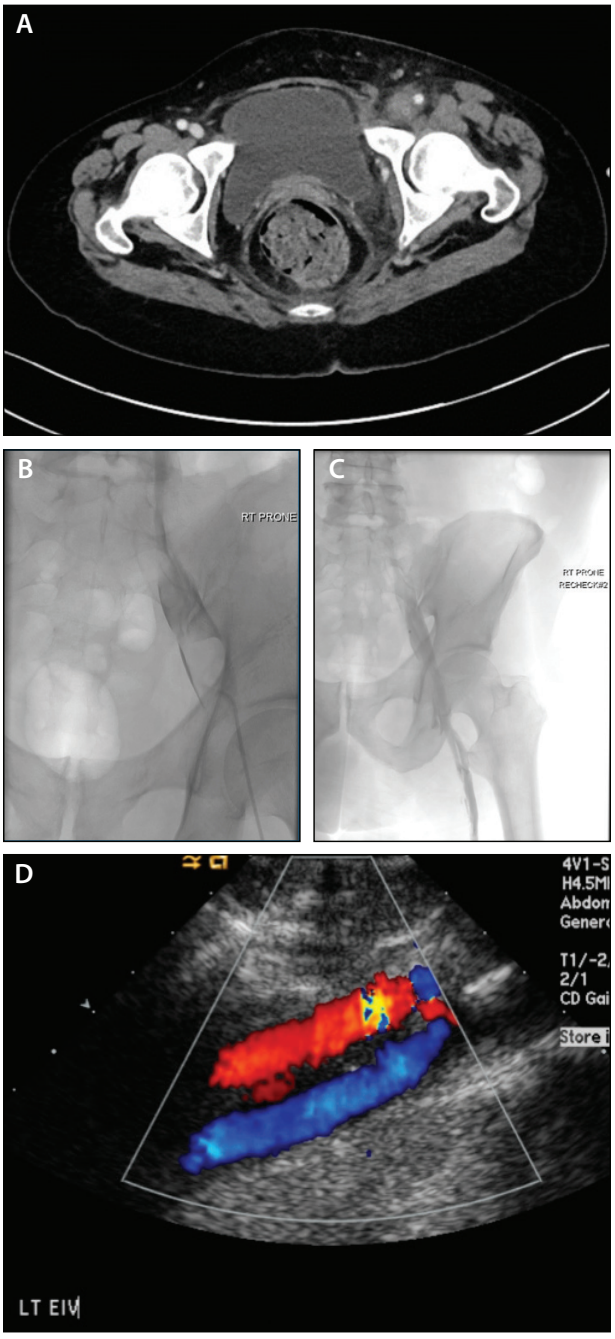

Figure 5. A 50-year-old man with sudden increased right-sided leg swelling after air travel. Ultrasound confirmed lack of flow in the external iliac vein confirming iliofemoral DVT (A), with injection venogram demonstrating significant clot burden in the right common iliac vein (B). TPA infusion initiated via infusion catheter (0.75 mg TPA/hour) with 24-hour recheck demonstrating patency with no stenosis (C). Follow-up ultrasound at 6 months (D) with novel oral anticoagulant demonstrated patency but required use of a class II compression stocking for symptomatic relief of mild post-thrombotic syndrome.

The 50-year-old man turned out to have had a hip replacement 2 weeks earlier and had not informed his medical team of his intended travel and was not on anticoagulation (Figure 5). To start, iliofemoral DVT should be established. Standard therapy for postoperative DVT is anticoagulation and continued use of graduated compression stockings.[1] Caution should be given toward more aggressive chemical lysis-based therapies due to increased risk of hemorrhage at the surgical site. Should catheter-directed therapies be pursued due to the severity of symptoms/extensiveness of DVT, consideration could be given to solely mechanical thrombolysis in the first instance.

CONCLUSION

As demonstrated by these case examples, the myriad of presentations and the need for personalized follow-up requires a dedicated group of individuals to commit to hospital-based algorithms based on evidence, expertise, and local institutional experience. The disparity between reported results of clinical studies emphasizes the fact that PMT strategies may not provide a clear benefit in all patients presenting with iliofemoral DVT, creating the need for personalized approaches.

Factors relating to outcome and risk/benefit analysis have not yet been clearly defined, however, losing the context of a patient-centered model of care while these factors are elucidated is not an acceptable approach to therapy. The management of iliofemoral DVT in the real-world setting has become more complex and as such, requires the development of a multidisciplinary program, not just perfection of any particular technique. ■

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Kicking the Can Down the Road: Why Recent Developments in DVT and PTS May Increase Cost of Care and Disease Burden in the Mid-21st Century

The benefits of rheolytic therapy with AngioJet™ ZelanteDVT™.

BY FEDOR LURIE, MD, PHD, RPVI, RVT

For many years, our understanding of venous thromboembolism (VTE) was based mainly on studies of arterial thrombosis. Recent animal models of deep venous thrombosis (DVT) and basic science research have uncovered new details of the mechanisms specific to venous thrombosis. Clinical trials of new anticoagulants and recent epidemiologic studies improved our understanding of VTE recurrence. Still, only a small group of researchers is endeavoring to shed light on the transition from acute DVT to chronic venous disease (CVD).

CONTINUUM OF CHRONIC VENOUS DISEASE

The open vein hypothesis has led to improved techniques and broader utilization of thrombolysis and mechanical and pharmacomechanical thrombectomy in patients with acute iliofemoral venous thrombosis. With treatment of more patients, it became apparent that a significant proportion of acute DVTs are recurrent events, and although thrombolysis is successful in resolving acute thrombi, up to 80% of patients have chronic lesions in the affected veins.[1]

Varicose veins are a known risk factor for DVT. A recent study showed that 66% of all patients with acute DVT have preexisting venous reflux.[2] This means that the majority of patients who clinically presented with acute venous thrombosis have either primary or secondary (post-thrombotic) preexisting CVD. This is not a new revelation; it is a well-known component of Virchow's triad—the damaged wall. However, it emphasizes an important aspect of the definition of CVD. CVD is defined based on the underlying pathology. For example, according to CEAP classification, a patient can have no clinical manifestations (symptoms or signs) but still have CVD provided there is identifiable venous obstruction or reflux. A patient with asymptomatic reflux in the superficial veins should be classified as C0a, Ep, As, Pr, whereas a patient with asymptomatic iliac vein obstruction should be classified as C0a, Es, Ad, Po.

Because of the high prevalence of venous reflux and wall changes in DVT patients, it is unclear if the reflux or obstruction detected after a DVT episode is post-thrombotic or if it is a manifestation of preexisting CVD. To answer this question, one needs to know if this pathology was present before the acute event or at least at the time of DVT, because changes in unaffected acute thrombus veins cannot develop acutely. In routine clinical settings, this information is usually unavailable. However, in clinical research studies, it is easily obtainable by performing standard venous insufficiency ultrasonography at the time of enrollment; yet, none of the major trials has attempted to do this. Not knowing the pre-DVT condition makes it impossible to correctly assess the natural history of the disease post-DVT. The symptoms and signs observed in patients after an acute event may be new or preexisting. The severity of preexisting symptoms may increase, remain the same, or even decrease after an acute DVT. Without knowledge of pre-DVT status, all changes are noted as the result of DVT, and the treatment outcomes in patients with preexisting CVD are lumped together with those who had no preexisting venous disease.

Primary disease develops at a young age[3] and remains subclinical for 20 to 30 years.[4,5] An estimated 37% of patients with reflux and no clinical manifestations within 13 years develop clinical class CVD of C2 or higher.[5] More than one-third of these patients progress to chronic venous insufficiency (CVI) in the following decade.[6]

It is estimated that at least half of all DVTs are asymptomatic. In some patients, the thrombus may spontaneously lyse with no visual damage to the venous wall and valves. In others, thrombus evolu-

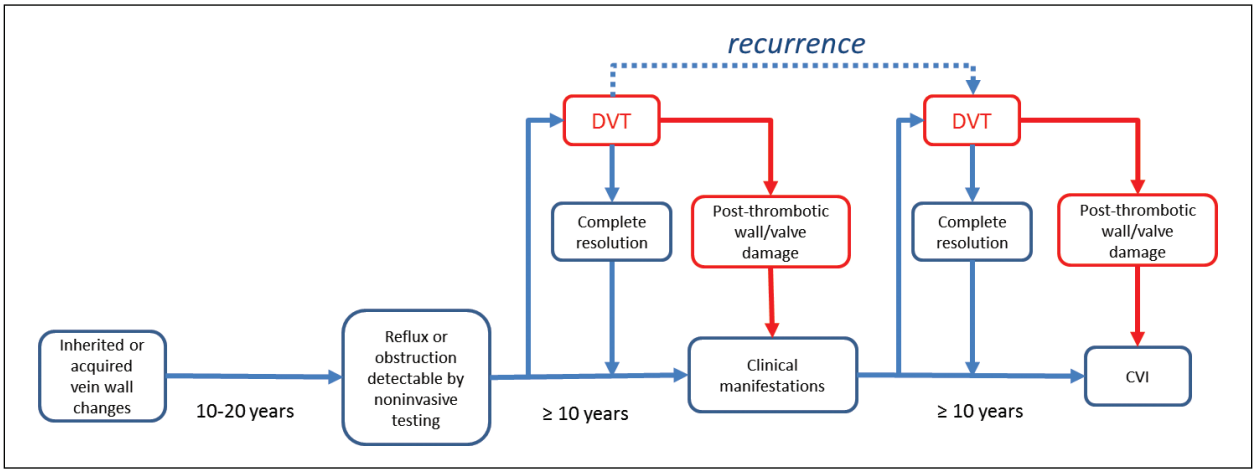

Figure 1. The continuum of chronic venous disease. The blue lines represent the expected natural history of the disease. The red lines represent acceleration of the natural history.

tion results in different degrees of venous obstruction, reflux, or both. In latter cases, an acute disease transitions to secondary CVD. The timing of subclinical stage of the secondary disease remains unknown, and unless a recurrent DVT or early clinical deterioration occurs, it remains in its latency for many years, similar to primary CVD. Thus, in the majority of the cases, acute DVT should be viewed as a continuum of CVD, not as an isolated event (Figure 1). In such patients, with complete lysis of the thrombus, they are simply returned to the previous stage of CVD and not to a healthy state. Newly developed post-thrombotic changes in these patients may accelerate the natural history of their CVD or the disease may remain latent for a long time. Considering these patients as healthy and not having venous disease is a mistake.

SHIFTS IN CLASSIFICATION AND TREATMENT

Pursuing simplification of trial logistics and cost savings, the majority of clinical trials evaluating CVD replaced the pathologic definition of secondary (post-thrombotic) CVD with a syndromatic definition of post-thrombotic syndrome (PTS). Instead of defining disease by the underlying pathology, certain severity scores have been used, such as the Villalta scale, Ginsberg scale, and Venous Clinical Severity Score. As a result, a patient with manifestations that are not severe enough would be classified as not having PTS. Although such definition can be justified, using this approach, patients with fewer symptoms but severe underlying pathology (eg, iliac vein occlusion) are classified as having a perfect treatment outcome or that treatment was not necessary. If such an approach were used in cancer, patients with early stages would be untreated, and treatment of symptoms would be considered a cure. Utilization of a severity score–based definition of disease in clinical trials has led to misclassification of patient outcomes. Although less symptomatic patients are misclassified as having been successfully treated, patients with preexisting CVD are misclassified as having poor outcomes even if their clinical manifestations were less severe but not below the threshold level.

Recent years are also marked by a shift toward ambulatory risk–based treatment of VTE. Current guidelines do not recommend immediate imaging and lean toward conservative therapy for the majority, if not all, DVT patients.[7] Availability of new oral anticoagulants makes this trend practical and sustainable. Clinical trials that use the severity-based definition of CVD and disregarded the clinical and pathologic manifestations of CVD prior to the acute episode contribute to this trend by denying the benefits of potentially effective treatment modalities. As the incidence of VTE is increasing, the likely result of this trend will be an increased number of patients with iliofemoral DVT who will reach the severity threshold and require treatment much later in life. Many of these patients who are now in their 40s and 50s will reach their severity threshold 15 to 20 years from now, making treatment more difficult and likely more expensive. This trend is also likely to shift the cost of treatment from private insurance to Medicare.

SUMMARY

Clinical guideline and medical policy writers and contributors should recognize the deficiencies of these clinical trials, and clinical investigators should consider a

more meaningful approach to defining post-thrombotic disease and clinical outcomes of treatment of acute venous thrombosis. ■

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The Continued Challenge of DVT Awareness and Education

A discussion about the barriers to patient referrals and interventionalists' need to own DVT treatment awareness and education.

WITH DEEPAK SUDHEENDRA, MD, FSIR, RPVI

From your perspective, what are the current barriers to patient referrals for evaluation of venous disease?

There are three main barriers to patients receiving quality venous care. The first is the perception within the medical community that venous disease is not important. Second, there is a lack of venous knowledge that exists on many different levels, from health care providers to patients, insurance companies, and the biomedical industry. The third barrier is a paucity of level I evidence for the management of venous disease.

Perception is everything. Most medical school students are not taught about venous disease. It is not uncommon to be told in anatomy class that the veins are not as important to learn as the arteries. Several years later, these same students are now the primary care providers caring for venous patients. Interestingly, when compared to the roughly 250 million cases of peripheral artery disease worldwide, venous disease is five to six times more prevalent and yet does not have a seat at the medical education dinner table. If a physician does not recognize the signs and symptoms of venous disease, then how can he/she refer a patient to a vascular specialist? Even if a patient is sent to a vascular specialist, it is not uncommon for that specialist to be an expert only in arterial disease and have very little knowledge of venous disease.

From the patients' perspective, many perceive venous disease as a cosmetic problem or a problem that cannot be treated (eg, post-thrombotic syndrome [PTS]) because they have not heard of such treatments from their primary care providers. On the other end of the spectrum, insurance companies play a large role as to whether patients receive proper venous care. It is not uncommon for insurance companies to minimize the morbidity and decreased quality of life associated with venous disease and deny coverage of venous treatment.

Finally, the dearth of level I evidence for the management of venous disease presents a significant problem in a health care climate that relies increasingly on data to determine coverage. Despite these barriers, I believe that the tide is turning and that venous education is permeating the medical community, albeit very slowly. In my experience, many patients are seeking out vein specialists on their own out of sheer desperation. After treatment, they are returning to their primary care providers and telling them about their experience. I can't tell you how many primary care providers have contacted me after our team treated their patient (who was not referred by their primary) to ask and learn about the treatments performed for deep venous or superficial venous disease. There is really a lot of after-the-fact education going on.

How can interventionalists overcome these barriers to widen referrals? What have been the most successful methods in your practice to establish awareness, education, and a well-developed patient care pathway?

Each specialty in the venous space brings a unique skill set to the table. The most important strategy to help overcome these barriers and widen referrals is to become an expert in venous disease, not just endovascular procedures.

When I look at how our deep vein thrombosis (DVT) practice at Penn Interventional Radiology (IR) has skyrocketed in the past several years, a lot of that growth has been through hitting the pavement and educating other physicians and hospitals. I started out by giving a lot of grand rounds at area hospitals for specialties such as critical care, internal medicine, orthopedics, neurosurgery, emergency medicine, and OB-GYN. I personally called the continuing medical education or medical staff office at various institutions and asked if they would be interested in a lecture on venous thromboembolism (VTE), and invariably I would get scheduled for a talk. Although the bulk of the talk would be on acute and chronic DVT, I also discussed pulmonary embolism (PE), inferior vena cava (IVC) filters, and superficial venous disease so they see Penn IR as a one-stop shop for anything venous related. Because nearly every physician has at least a few patients with PTS, our DVT practice has grown significantly from chronic DVT referrals.

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Why is it important for interventionalists to be responsible for driving this awareness and education?

Interventionalists gain extensive experience on the venous system during their careers from performing venous access to more complex chronic DVT recanalization procedures. They see first-hand the complications of deep venous obstruction, whether it be from VTE or venous access catheters. Because they are called upon to manage these complications, it is fitting that they be at the forefront of venous care and education. However, being able to technically perform complex venous procedures does not make one an expert in diseases of the veins. Just as it is paramount for the interventionalist practicing peripheral artery disease or interventional oncology to know everything about the disease process, the vein expert must be equally knowledgeable to provide care for all facets of the disease.

What do referring specialties need to know about DVT, PTS, and early intervention options and benefits? How does education differ by specialty?

First and foremost, the basics of VTE management (anticoagulation, compression therapy, and indications for IVC filters) need to be discussed, because there is still much confusion over these issues. One such example is length of anticoagulation for a provoked DVT. It is not uncommon to see a nonhypercoaguable patient with a history of provoked DVT over 10 years ago continue to be on anticoagulation because the referring physician is fearful of discontinuing the medication. Taking an anticoagulant in my opinion is not insignificant, and bleeding complications can occur in any patient.

Although educating referring physicians about endovascular treatment options and available level I evidence is important, even more paramount is that they have someone or someplace to turn to (eg, office number, cell phone, email) when they need help or feel that the patient's problem is outside their scope of practice. With the increasing demands of seeing higher volumes of patients, primary care providers and other specialists do not have the time or even the proclivity to keep up with all areas of medicine and often have to refer patients to specialists. Even more challenging is when patients present with complications from DVT, and the vascular specialist says, "There's nothing to do." Where does that leave the primary care physician? One of the things I emphasize to referrers is that their job is not to determine whether a patient is a candidate for endovascular intervention but rather to remember that Penn IR is a place that they can turn to for help.

VTE is encountered in every specialty. We assume that some specialists, hematologists for example, would be familiar with endovascular procedures for chronic DVT, but surprisingly, it is not often discussed in their training. We work very closely with the Penn Thrombosis Center, and it has been a very symbiotic relationship, especially for patients with chronic DVT and/or IVC filters requiring complex retrieval methods. After discussions with the Penn Thrombosis Center regarding our interventions for chronic DVT, which they were not familiar with, we now have a steady referral base and are able to not only improve the lives of those with PTS but also ensure that they are receiving the very best care from a medical management standpoint at the Penn Thrombosis Center.

Finally, it is becoming more evident that there needs to be a standard curriculum in venous disease in our interventional radiology, interventional cardiology, and vascular surgery training programs. Many of us (and the public) assume that because a physician has experience with one disease process, such as arterial disease, that they have experience with venous disease. While the skill set required for both conditions is similar, venous disease is different, and the knowledge we have from arterial disease cannot be entirely extrapolated to venous disease.

What do patients need to know about venous disease?

VTE is the third major cause of cardiovascular death behind heart attacks and strokes, but very few people have heard of DVT or PE. Increased public awareness about the signs, symptoms, risks, and long-term complications of DVT is needed. For those with chronic complications from VTE such as PTS or chronic thromboembolic pulmonary hypertension, patients should know about potential options that may be available to them that can significantly improve their quality of life.

Likewise, superficial venous disease affects 25% of the population, and the incidence is much higher in those with a history of extensive DVT. The vast majority of patients are unaware that chronic venous insufficiency (CVI) is more than just varicose or spider veins. CVI is a disease spectrum that, if left untreated, can lead to long-term disability, decreased quality of life, and significant health care expenses.

Is a multidisciplinary approach to DVT treatment necessary or valuable? What is the impact on both the patient and hospital system?

Absolutely. We all bring different strengths to the table, and each specialty has their own valuable expertise to offer DVT patients. Our team works closely with hos-

pitalists, hematologists, oncologists, intensivists, cardiologists, podiatrists, physical therapists, and the lymphedema team. Just as a tumor board helps to bring together experts in oncology care, a multidisciplinary approach to VTE is essential to treating all aspects of the disease, minimizing complications, establishing a patient care pathway, and educating providers as well as patients.

VTE is the most common cause of preventable hospital death, and hospitals are now being graded on their incidence of DVT, which can ultimately affect reimbursement. Currently, CMS does not reimburse hospitals for DVT or PE that occurs in association with hip or knee replacement. Instituting a multidisciplinary team approach to DVT enables a hospital to reliably collect data and performance measures, form a quality improvement program, develop standardized protocols for VTE risk assessment and prophylaxis, and improve patient outcomes and thereby indirectly improve the bottom line. Furthermore, by having a patient plugged into a multidisciplinary system for DVT management, patients are potentially less likely to use the emergency room for complications such as PTS. With a modest amount of resources and, most importantly, if DVT is treated like a disease state, a hospital has the ability to become a venous referral center that can translate into providing the full spectrum of services for venous disease, from superficial venous disease to iliocaval reconstruction and complex IVC filter removal

How do you develop a multidisciplinary team and create a good patient care pathway?

Networking with colleagues in your institution is key. You have to find a friend in each specialty and reach out to him or her and say, "This is what I would like to do, and I would love if you would partner with me to improve patient care in our institution." If you can find other specialists who have an interest in DVT or are passionate about improving patient care in the hospital, then you have the nuts and bolts of a multidisciplinary team. A great place to start is to get involved with the anticoagulation committee in your hospital.

Because the ER is traditionally on the front lines of seeing acute DVT cases and is constantly under scrutiny for triage efficiency, establishing a patient care pathway that aims to improve triage efficiency is valuable. Penn IR established a pathway with the ER and it has not only expedited care for DVT patients but also ensured that they receive proper follow-up care upon discharge.

Who should own patient education on DVT?

I don't think one specialty owns DVT education, but I think the three main specialties are primary care/hospitalists, vascular specialists, and hematology/oncology. The primary care physician should be aware of the warning signs of DVT, how DVT is diagnosed, and where to refer the patient as soon as the diagnosis is made. If a patient is admitted with DVT, then the hospitalist should be familiar with the risks and benefits of anticoagulation, IVC filters, and endovascular therapy. It's important to remember that not every patient is a candidate or will benefit from an endovascular treatment. Therefore, hematologists play an extremely important role in the management of DVT because anticoagulation remains the foundation of therapy. The responsibility of educating the patient and their family about DVT lies, in my opinion, with the physician who will be following the patient long term for their DVT.

If an intervention is to be performed, then there is no question that the interventionalist will play a key role in long-term care and DVT education. I also believe that patients should be encouraged and provided resources to educate themselves about their medical condition.

What is important for patients to know both before and after the intervention?

An intervention is just the beginning of what may be a long journey. Although many patients will notice significant improvement after undergoing an endovascular procedure, there are some who may not. The most challenging patients are those who have a genetic predisposition to clotting because many times, no matter what you do, their genetics make them prone to recurrent DVT. That can be very difficult for patients to comprehend, especially for young patients who will have to deal with thrombosis issues for the rest of their lives.

Patients must also understand that anticoagulation has to be followed to a "T." That is their lifeline. Missing just one dose can have disastrous consequences.

If a patient is told that nothing can be done, I advise him or her to get a second or third opinion, preferably from a physician or center with a lot of experience in venous disease. The majority of patients who come to Penn IR have been told that nothing can be done by other vascular specialists, and for many of these patients, we are able to recanalize their deep veins and have a positive impact on their lives. ■

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CASE REPORT

Complex Thrombectomy of Chronic Deep Vein Thrombosis

BY S. JAY MATHEWS, MD, MS, FACC

A 72-year-old woman with a history of diabetes, dyslipidemia, hypertension, and previous right lower extremity deep vein thrombosis (DVT) presented with progressive left lower extremity swelling. The patient was originally treated 3 years earlier for unprovoked DVT with warfarin, which was discontinued after 6 months. She underwent uncomplicated ventral hernia surgery 6 weeks prior to her office visit. Two weeks after her surgery, she developed painful left lower extremity swelling and was found on venous duplex ultrasound to have extensive DVT involving the common femoral vein to the infrapopliteal veins. She was managed conservatively with intravenous heparin. A permanent inferior vena cava (IVC) filter was placed by her surgeon due to concerns over potential bleeding risk in the postoperative setting. She was discharged on oral rivaroxaban. Due to progressive, severe post-thrombotic syndrome (PTS), she was referred to my clinic by her primary care physician.

EXAMINATION AND INITIAL THERAPY

The patient's initial exam was notable for marked unilateral left lower extremity swelling (Figure 1). She reported daily pain with ambulation despite medications. There were few varicosities noted. Edema was seen even in the morning. There was recent skin pigmentation with mild inflammation and erythema. Extensive induration with recent onset of one small weeping venous ulceration was also noted. She was mostly compliant with compression stocking therapy (although she was in light uniform compression from the hospital setting). Based on these findings, she was noted to have C6 disease according to the CEAP classification with a Venous Clinical Severity Score (VCSS) of 18.[1,2]

Discussed treatment options included ongoing conservative management with anticoagulation and stronger compression stocking therapy (thigh-high measured graduated compression stockings of at least 20 to 30 mm Hg strength) versus interventional therapy. Due to her symptoms, the patient opted for the latter. She was maintained on rivaroxaban throughout her procedure and started on appropriate compression stocking therapy immediately.

INTERVENTIONAL PROCEDURE

The original treatment strategy was to attempt same-day therapy utilizing the 8-F AngioJet™ ZelanteDVT™ catheter (Boston Scientific Corporation) in combination with Power Pulse™ spray of alteplase (Genentech), a recombinant tissue plasminogen activator (tPA), into the chronic thrombus. The ZelanteDVT is a dual-lumen device that performs rheolytic thrombectomy via delivery of high-velocity pulsatile saline jets that help macerate thrombus.[3] The port can also be rotated to direct the thrombectomy (Figure 2). Power Pulse therapy allows delivery of physician-specified agents (usually a thrombolytic) into thrombus in a pulsatile fashion.[4]

On the first day, access was achieved in the right common femoral vein with the intention of going to the contralateral side for treatment over the iliac vein bifurcation. Direct access of the left popliteal vein (despite being thrombosed) could have been possible if we did not have to address extensive infrapopliteal thrombus as well. In our experience, if the inflow into the femoral vein is not established, the declotted segment can rethrombose rapidly due to stasis. Unfortunately, accessing the contra-

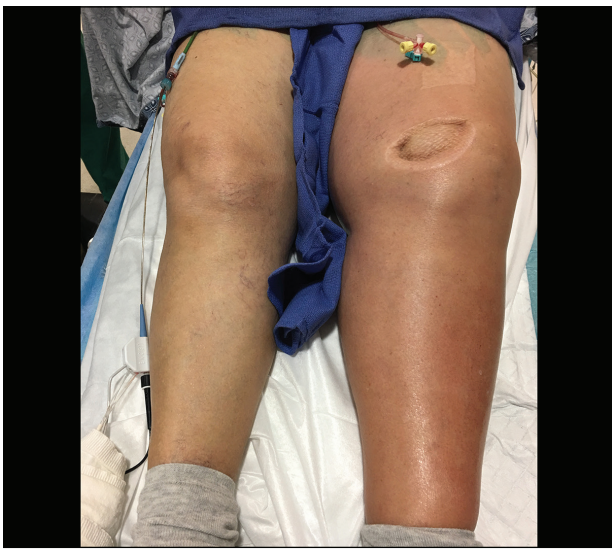

Figure 1. Initial presentation to the cardiac cath lab with marked swelling of the left lower extremity.

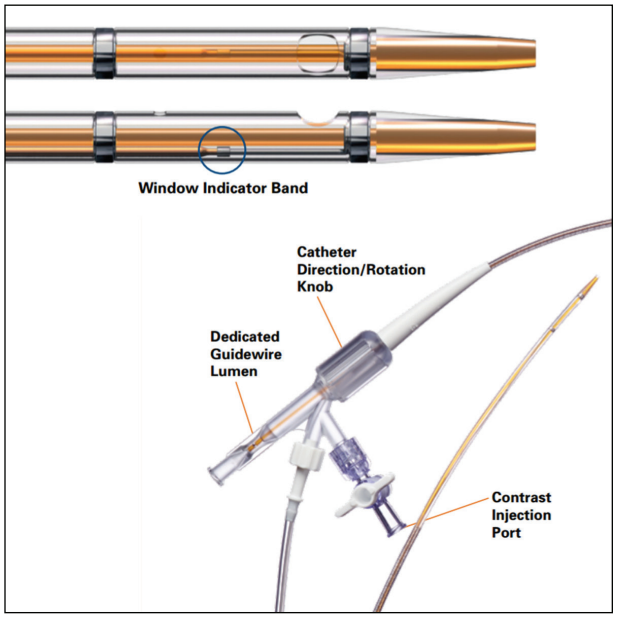

Figure 2. The AngioJet ZelanteDVT catheter.

lateral limb with a 5-F Contra catheter (Boston Scientific Corporation) and a hydrophilic guidewire was not possible due to apparent thrombosis of the entire left iliac venous system, which was not appreciated on previous outpatient imaging (Figure 3). We decided to perform ipsilateral pharmacomechanical catheter-directed thrombolysis (PCDT). The left common femoral was accessed within the thrombosed segment, and Power Pulse spray was performed using the ZelanteDVT catheter (16 mg of tPA in 50 mL normal saline instilled into the occluded segment from the left common iliac to the common femoral vein). After 45 minutes, we performed pharmacomechanical thrombectomy (PMT) with the ZelanteDVT catheter to remove thrombus. Intravascular ultrasound (IVUS) confirmed dense fibrotic changes and compression due to an overriding iliac artery (Figure 4). The presence of extensive May-Thurner syndrome (iliac vein compression) was likely a contributing factor to the patient's extensive thrombosis.[5] Additional balloon angioplasty was performed with an 8- X 200-mm noncompliant balloon at 20 atm, which created a reasonable outflow channel (Figure 5). We then were able to access the contralateral side from the right groin, using a crossing catheter to carefully navigate through the chronically thrombosed femoral vein until we could identify a patent infrapopliteal segment (Figure 6). A 50-cm EkoSonic MACH 4 catheter (BTG International) was deployed across the treatment zone infusing 1 mg tPA for 16 hours along with low-dose heparin.

The next day, we used the ZelanteDVT catheter to perform PMT from the level of the distal veins back into the femoral vein (Figure 7). An 8- X 200-mm noncompliant

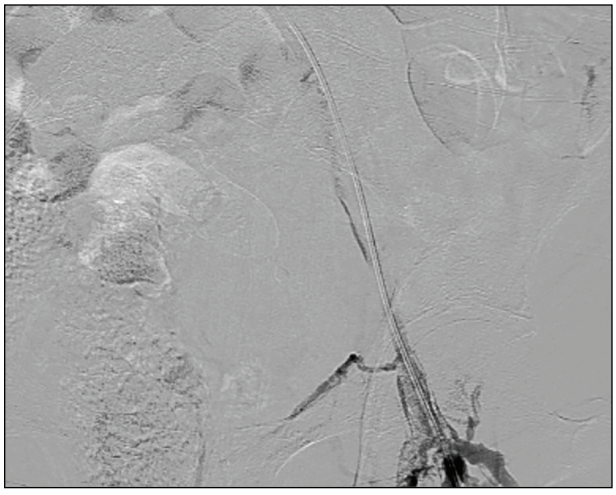

Figure 3. Occlusion of the left common iliac vein.

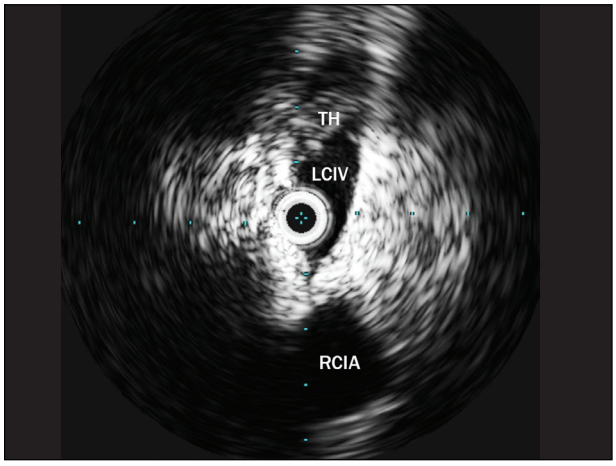

Figure 4. IVUS of the left common iliac vein demonstrating compression consistent with May-Thurner syndrome with overriding right common iliac artery. Abbreviations: LCIV, left common iliac vein; RCIA, right common iliac artery; TH, thrombus.

balloon was used for serial inflations in the femoral vein and a 10- X 80-mm balloon at the level of the common femoral vein. IVUS revealed that the compression originated at the level of the external iliac vein into the ostium of the common iliac vein. Access was achieved in the left common femoral vein, and a 16- X 90-mm self-expanding stent was deployed from the common to external iliac veins, postdilated distally with a 12-mm balloon and a 14-mm balloon proximally (Figure 8). IVUS revealed excellent wall apposition and resolution of compression. Final IVUS imaging confirmed no residual thrombus.

FOLLOW-UP

At her 2-week follow-up, the patient demonstrated remarkable recovery and improvement of symptoms. She reported no pain with ambulation, mild varicosities, edema

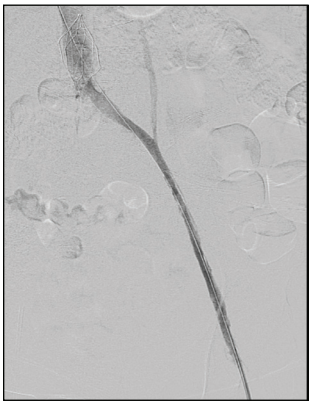

Figure 5. After balloon angioplasty of the left iliac veins.

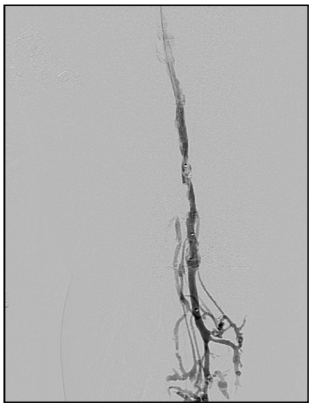

Figure 6. Left infrapopliteal venogram demonstrating femoral venous occlusion and patent distal segment.

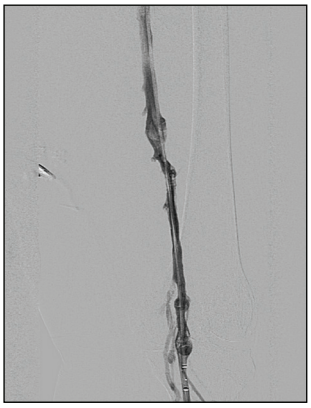

Figure 7. AngioJet ZelanteDVT of the left femoral vein.

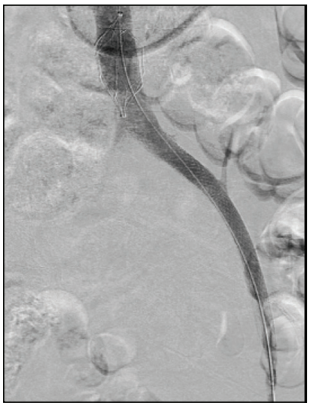

Figure 8. Post-iliac vein stenting with resolution of compression.

only in the late afternoon/evening, limited old pigmentation with no inflammation, mild induration without ulceration, and some compliance with compression stockings (C3, VCSS 6) (Figure 9). She was maintained on anticoagulants and scheduled for surveillance ultrasonography of her iliac vein stent and femoral veins at 3 and 6 months. Compliance with compression therapy was also reinforced.

DISCUSSION

Management of chronic or acute on chronic venous thrombosis can be challenging, because it may require a multimodality approach to achieve procedural success and symptomatic improvement. At our institution, the 8-F ZelanteDVT catheter remains a cornerstone of therapy, but it is at times combined with other technologies. In the setting of acute thrombosis (generally < 2 weeks), PCDT with AngioJet can be very effective and can offer same-day DVT therapy.[6] We have found that waiting at least 30 minutes or more will allow for more effective fibrinolysis within the thrombus. Maceration of the thrombus with a balloon prior to fibrinolysis may also increase efficacy. Even patients who are deemed poor candidates for systemic thrombolysis may still benefit from local thrombolysis, because little escapes into the systemic circulation.[7] We have successfully treated postsurgical patients, including those with orthopedic injuries or major intraperitoneal operations suffering from acute DVT with this method. For those who truly cannot receive thrombolysis, ZelanteDVT without thrombolytic- or nonlytic-based devices can be used, including the ClotTriever (Inari Medical Inc.) and Indigo CAT8 (Penumbra, Inc.) catheters. However, adjunctive therapy with the ZelanteDVT is often necessary to facilitate residual clot removal. Rotational devices like the Cleaner 15 or Cleaner XT (Argon Medical Devices, Inc.) macerate thrombus without extraction. They are perhaps used more effectively when in conjunction with a thrombectomy catheter like the ZelanteDVT to remove the residual debris rather than allowing it to embolize to the lungs.

Chronic thrombosis presents a therapeutic challenge, given the nature of the thrombus and recalcitrance to treatment. Organized clot can eventually remodel, making it resistant to even prolonged balloon angioplasty and extraction. Moreover, occluded veins can experience intimal hyperplasia, which may affect thrombolysis outcomes.[8] Chronic thrombus can, however, have mixed morphology that may make it amenable to fibrinolytic therapy. In our institution, we will use Power Pulse thrombolysis with the ZelanteDVT catheter and/or overnight, acoustic pulsed thrombolytic therapy with the EkoSonic device. In the setting of EKOS, we will usually go back with the ZelanteDVT catheter the next day to remove softened clot. We have also had excellent experience in using the Indigo CAT8 device to "cork" pieces of chronic thrombus not responsive to initial rheolytic therapy. Though effective in extracting dense clot, this process can be time consuming. It is most effective when the 8-F or greater sheath is placed in close proximity to the thrombus, preferably with a removable valve to facilitate clot extraction from the sheath. The AngioVac device (AngioDynamics) is also useful, typically for massive thrombosis, but is limited by needing a perfusion circuit and large-bore venous access, usually via the internal jugular. Inadequate flow through the circuit will limit the amount of thrombus removed. In addition, this device in its current iteration typically cannot be brought down into the infrainguinal femoral vessels due to size and working length constraints. Although we have used this

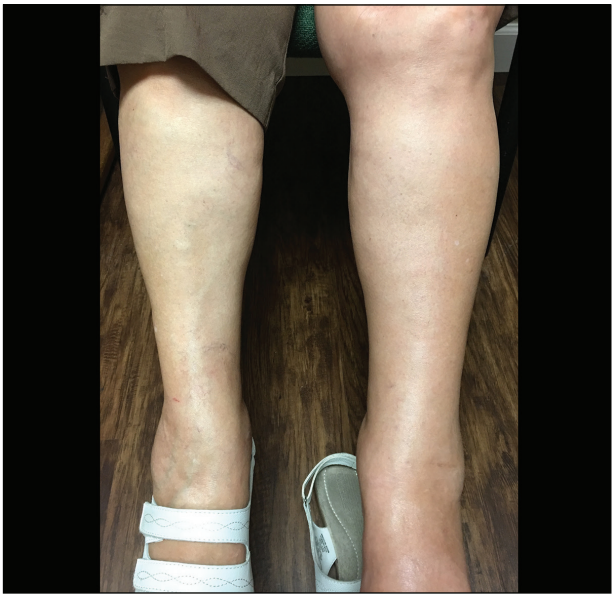

Figure 9. Left lower extremity on follow-up demonstrates visual improvement.

device within thrombosed iliocaval/iliofemoral vessels (often with a thrombosed IVC filter), we have also used ZelanteDVT effectively in larger iliac veins. Other than for iliocaval or iliofemoral compression, we do not use stents for chronic thrombosis (eg, below the common femoral veins), mostly due to a paucity of data and lack of venous-specific platforms.[9,10] Concerns remain regarding migration, fracture, thrombosis, and long-term patency within the femoral veins.

With the number of tools now available with relative ease of use, safe operation is exceedingly important. For example, with powered aspiration devices not on a continuous circuit (eg, Indigo CAT8), there is a concern regarding rapid blood loss when outside of thrombus and in open vessel. This requires care to make sure that the device is deactivated when outside of clot. This is less of a concern with AngioJet devices because they are isovolumic, meaning that the blood removed is equal to the amount of saline administered; the volume aspirated is approximately 1 mL/s. However, one can achieve prolonged run times during massive thrombosis cases. Hematuria (due to hemolysis) is common, but rarely clinically significant and usually can be managed with hydration. Significant hemoglobinuria with renal dysfunction requiring urine alkalinization (eg, with sodium bicarbonate) is uncommon.[11,12] This may potentially be avoided if thrombectomy is limited only to occluded venous segments. Despite the hematuria, anticoagulation should not be stopped when it is seen postprocedure, as venous rethrombosis is a concern. Pancreatitis is also very rare and usually resolves with adequate hydration.[13] We have seen this only in patients with very prolonged run times. Boston Scientific has run time guidelines for each of its catheters. Bradycardia has been reported with rheolytic therapy. Usually, this is uncommon in the treatment of lower extremity DVT.[14] Routine pretreatment for bradyarrhythmias is not recommended.[14]

Management of symptomatic DVT remains an evolving field. A multimodality approach to interventional therapy coupled with best medical practices can offer meaningful quality-of-life improvements in appropriately selected patients. ■

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CASE REPORT

Managing the Challenges of Extensive Thrombus Burden Involving the IVC

BY VINCENT DIGIOVANNI, DO, FACOS, RPVI, AND ROBERT J. MEISNER, MD, FACS

This case study illustrates the removal of considerable occlusive thrombus burden from the inferior vena cava (IVC) around an indwelling IVC filter and the iliac veins in an elderly patient with multiple comorbidities. The procedure was done under monitored anesthesia care with discharge to home the same day.

CASE PRESENTATION

An 85-year-old man presented to our outpatient clinic with severe bilateral lower extremity swelling, skin texture and color changes, and inability to ambulate even short distances due to thigh and calf claudication. Symptoms were present for approximately 2 months with increasing severity. He had an IVC filter insertion 4 years prior for a deep vein thrombosis (DVT) in his right lower extremity with inability to anticoagulate due to a now-resolved GI bleed. A recent ultrasound performed in his primary care physician's office demonstrated an occlusive thrombus in his right common femoral vein. On evaluation, he had very tense and tender calves and thighs with significant venous stasis changes noted in both ankles and small preulcerative lesions at the right medial malleolus. Pulses were not palpable due to his edema, but he had multiphasic Doppler signals in both legs, and his feet were warm with pink coloration. His medical history is significant for hypertension, hyperlipidemia, chronic obstructive pulmonary disease, and coronary artery disease. A repeat venous duplex demonstrated occlusive DVT in both lower extremities at the common femoral veins and multiple venous collaterals in the thighs and pelvis. A CTA scan of his abdomen and pelvis performed 4 months previously was reviewed and did not demonstrate any iliac vein or IVC thrombosis, nor retroperitoneal masses. Ankle-brachial index values in the office with exercise were within normal limits. Given the amount of edema present in the patient's legs with symptoms of venous claudication, the decision was made to proceed with venogram and possible thrombolysis.

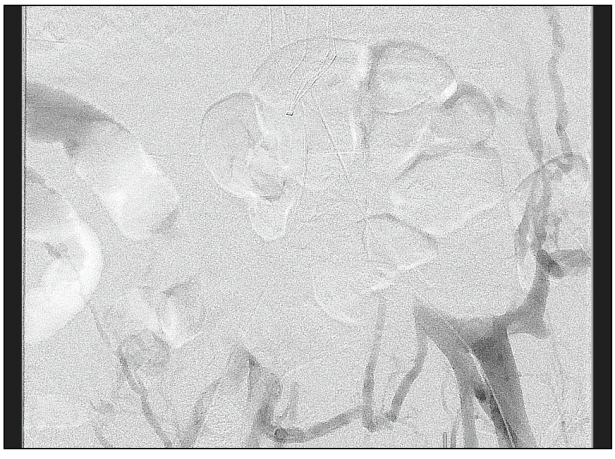

Figure 1.

TREATMENT TECHNIQUE

The patient was brought to the outpatient catheterization lab, and after repeat evaluation with venous ultrasound, he was placed supine on the treatment table. Monitored anesthesia care (local anesthesia and sedation) was administered. Access was achieved bilaterally in the mid-superficial veins with 8-F sheaths under ultrasound guidance. Initial imaging with ultrasound showed noncompressible common femoral veins. Hydrophilic guidewires were advanced through the semi-soft thrombus in the iliac veins and the more chronic thrombus in the IVC. Initial venography demonstrated an occluded IVC and proximal iliac veins (Figure 1). The common femoral vein on the left was patent, and numerous collaterals were present in the pelvis providing drainage from both legs to the azygos system. A low-lying and distorted Optease IVC filter (Cordis, a Cardinal Health company) was present within the occluded IVC, and organized thrombus extended above the IVC filter (Figure 2). An 8-F AngioJet™ ZelanteDVT™ thrombectomy catheter was used to Power Pulse™ the thrombus from proximal to distal through the iliac veins with 10 mg TPA in 100 mL normal saline solution using both superficial femoral vein access points to treat the respective occluded Iliac veins. After 30 minutes of dwell time, thrombectomy was performed of the occluded segments. A total treatment time of 200 seconds was performed within the venous system, and immediate follow-up venogram demonstrated now-patent vessels (Figure 3). IVUS evaluation was performed

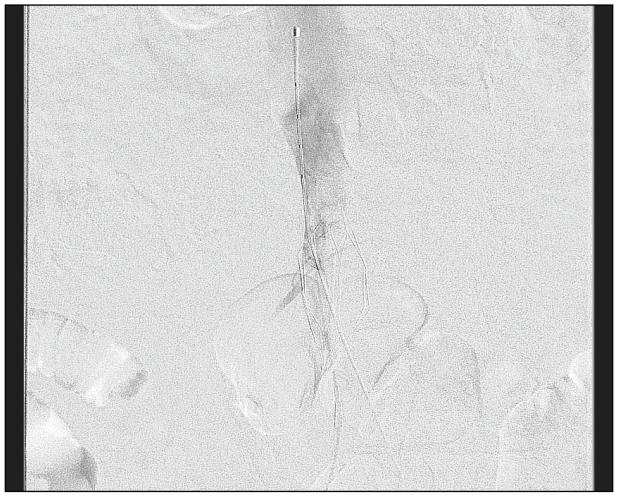

Figure 2.

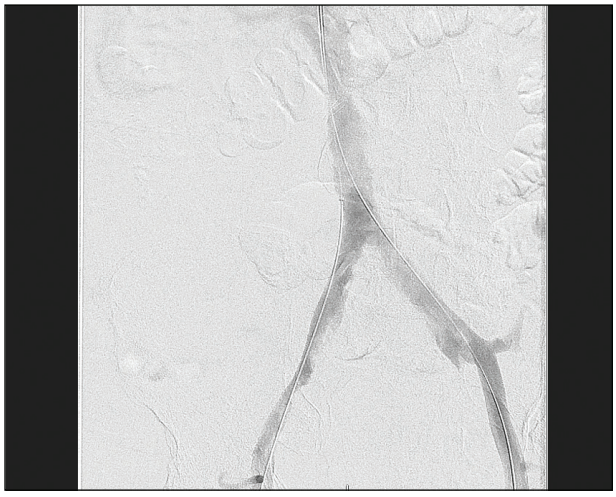

Figure 3.

through both access points into the infrarenal IVC and did not demonstrate any evidence of caval or iliac vein narrowing. No angioplasty was performed on the venous system. Both sheaths were removed in the holding area without complications. The patient's legs were wrapped from the ankles to the thighs with elastic bandages. After 2 hours of recovery, the patient was discharged home with oral anticoagulation. On the follow-up telephone call the next day, the patient reported mild hematuria that was dissipating and no significant pain in either access location. Upon presentation in the clinic 14 days postprocedure, he had lost 22 pounds, his legs were no longer edematous, and he was ambulating without pain. Following consultation with hematology and his primary care physician, he was brought back to the interventional lab 4 weeks later for laser extraction of his embedded IVC filter. Although he has no evidence of inherited thrombophilia, the patient will be maintained on anticoagulation indefinitely due to the risk of rethrombosis. He is also taking low-dose aspirin for his cardiac issues.

DISCUSSION

IVC thrombosis is an underrecognized disease process, likely as a component of insufficient imaging. Venous ultrasound fails to adequately image the intra-abdominal IVC and the proximal iliac veins; and CT, if not done with a venous phase, may fail to identify acute thrombus or external compression. Previously thought to be the sequelae of a hypercoagulable state, IVC occlusion is reported as a consequence of indwelling IVC filters in 10% to 15% of patients with long-standing caval interruption. Other reasons for IVC thrombus include malignant and nonmalignant compression or encroachment of the cava, abscesses, hematoma/trauma, and hemodialysis. At its core, IVC thrombosis and occlusion can be viewed as an extension of lower extremity DVT, which causes more severe edema/ulceration and venous claudication. In symptomatic individuals, treatment can be successfully undertaken through endovascular means even with chronic clot and with/through an indwelling IVC filter. The ZelanteDVT catheter, with its increased infusion and extraction abilities over previous generations of mechanical thrombectomy catheters, allows for the safe removal of considerable thrombus burden within the veins.

Access in patients with proximal DVT and lung disease is always challenging, because they are often unable to tolerate prone positioning. It has been our practice to obtain access at the superficial femoral vein if the patient is unable to lay prone for venous treatment, as this access point establishes excellent sheath "purchase" to allow for common femoral vein imaging and device leverage for diseased proximal segments. Even large sheaths (11 F) in this area are associated with few site complications. We typically remove sheaths from the mid-superficial femoral veins in the holding area after ACT values drop under 200, but even these can be removed safely in patients receiving full anticoagulation if care is taken to compress the vein puncture locations appropriately. ■

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CASE REPORT

Single-Setting Treatment for Iliac DVT

BY ROBERT J. MEISNER, MD, FACS, AND VINCENT DIGIOVANNI, DO, FACOS, RPVI

A 45-year-old African American woman presented to the emergency department with an approximately 1-week history of left thigh swelling and left-sided pelvic pain. She had undergone an abdominoplasty operation 2 months prior that was otherwise uncomplicated. The emergency department staff performed an abdominal and pelvic CT scan with IV contrast. They diagnosed a left-sided iliac vein thrombus based on the CT scan (Figure 1).

The patient travels for work with intermediate-length flights, and she had traveled twice in the previous week. Otherwise, she did not have any risk factors for deep vein thrombosis (DVT)—no prior DVT and no family history of hypercoagulability. The relatively recent surgery may have contributed as well. The CT of the pelvis suggested a typical May-Thurner compression physiology at the level of the proximal left iliac vein (Figure 2); the thrombus was in the associated area and distal to that compression point.

The emergency department started the patient on IV heparin and admitted her to the hospital at that time; she was admitted in the early morning around 5:00 AM. We kept her on nothing by mouth and added her on the procedural schedule in the hybrid operative suite.

TREATMENT TECHNIQUE

The patient was brought into the hybrid OR in the afternoon of the same day. Local anesthesia and conscious sedation was planned for and used. She was placed in a prone position, and the left popliteal fossae was prepped and draped. The left popliteal vein was visualized and cannulated with ultrasound guidance, and we upsized immediately to an 8-F sheath. Peripheral left femoral-popliteal venogram demonstrated no thrombus in this segment (Figure 3). An angled hydrophilic catheter was advanced proximally, and the left iliofemoral segment showed partial density filling of the vein at this segment (Figure 4). Over a stiff hydrophilic guidewire, we advanced an 0.035-inch digital intravascular ultrasound (IVUS) catheter. The IVUS images revealed a nearly occlusive thrombus occupying the majority of the lumen of the left external iliac and mid-iliac vein; the proximal common iliac vein showed a tapered tongue of thrombus extending to a drastically compressed proximal left common iliac vein. There appeared to be a double compression, where both the left and the right common iliac arteries were visualized as culprit compressive entities (Figure 5).

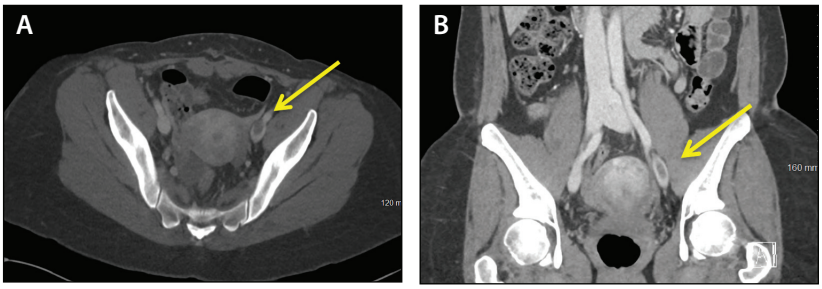


Figure 1.

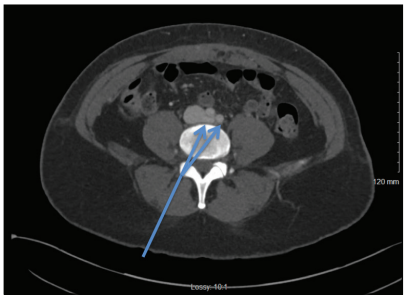


Figure 2.

Figure 3.

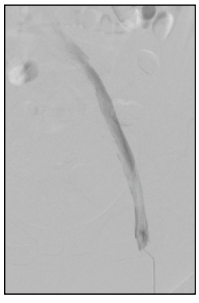
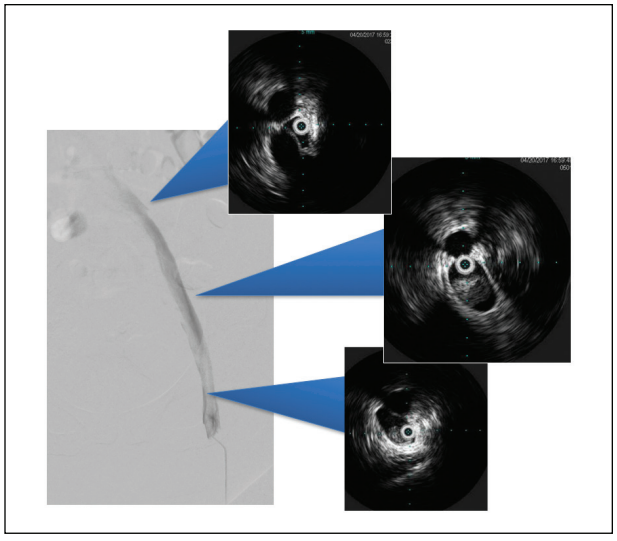


Figure 4.

Ten milligrams of tPA alteplase was prepared in a 100 mL bag of normal saline. The 8-F AngioJet™ ZelanteDVT™ (Boston Scientific Corporation) catheter was loaded over the wire. We used the thrombectomy mode first for < 20 seconds along the length of the thrombus. We then transitioned into Power Pulse™ mode and pulsed all 100 mL (10 mg) of the tPA into the thrombotic segment. We then waited for 30 minutes.

After 30 minutes, we went back in with the ZelanteDVT catheter in thrombectomy mode. We performed thrombectomy for between 220 and 230 seconds and then



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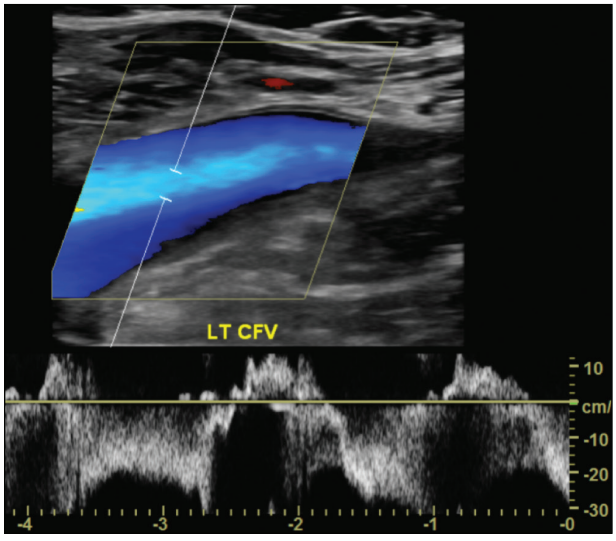

Figure 9.

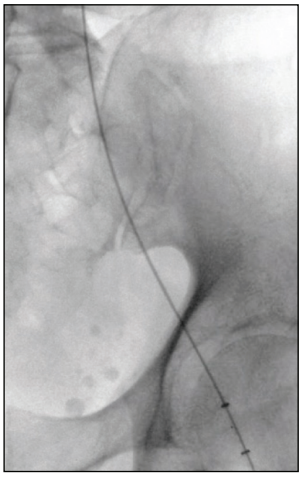

Figure 6.

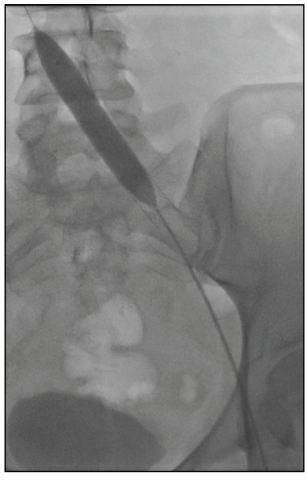

Figure 7.

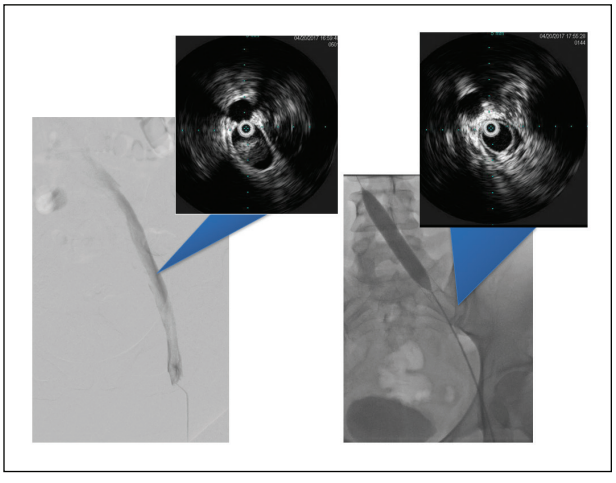

Figure 10.

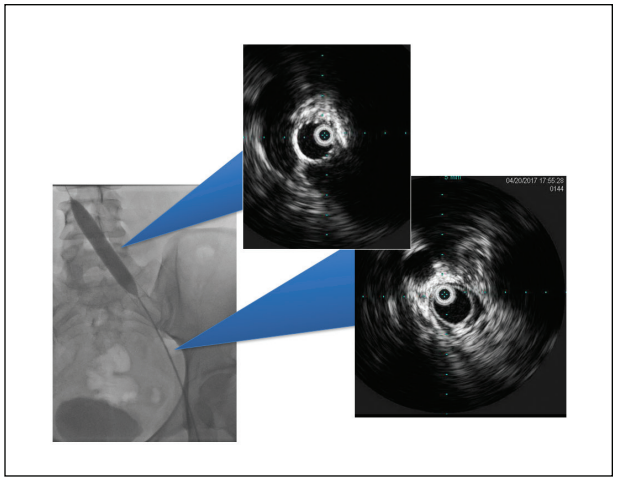

Figure 8.

reevaluated with IVUS. Traditional venography would not be sensitive to residual thrombus. There was posterior residual thrombus seen in the left common femoral vein. We utilized the directionality of the ZelanteDVT catheter, rotating the window toward the area of residual posterior thrombus and repeating the thrombectomy action for an additional 10 to 20 seconds.

We were satisfied to see the thrombus responded very well to the treatment; it was completely thrombus-free after therapy. We did make anatomic notes about the extensive compression using the IVUS catheter at this point. We up-sized to an 11-F sheath over a Magic Torque™ guidewire (Boston Scientific Corporation). We used a self-expanding stent extending from the inferior vena cava to the mid-left iliac vein and postdilated the stent with an angioplasty balloon (Figure 7).

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We used IVUS to reevaluate the anatomy after intervention (Figure 8). We found that in this case, there was essentially very little use in repeating digital-subtraction venograms; the sensitivity to identify partially occlusive thrombus and compression is low with venogram only. Instead, our practice has been to use IVUS imaging exclusively. In fact, we completed this case in under 90 seconds of total fluoroscopy time.

The wires, catheters, and sheaths were removed, and manual pressure was held. Elastic bandages were used, and the patient was put on bedrest for 3 hours. She was given clopidogrel (300 mg) and aspirin (81 mg) in the post-anesthesia care unit. She was fed dinner and prior to discharge was started on a 21-day loading dose pack of rivaroxaban and given a script for 20 to 30 mm Hg gradient compression garments. She was discharged in the early evening on the same day as her admission.

At 1-month follow-up, ultrasound imaging showed patency of her iliac stent (Figure 9).

CONCLUSION

The size and utility of the ZelanteDVT catheter has given us greater ability to treat patients in a more thorough and complete manner even in a single interventional setting. The directionality feature is a nice update over previous generations of catheters, and it is useful for more organized residual thrombus. We have also found that first running the catheter relatively quickly through the thrombus on thrombectomy mode, then going to Power Pulse mode, waiting, then performing a final thrombectomy run, we have a more useful debulking of the thrombus. We would reemphasize the need to use IVUS as the primary imaging modality in directing therapy through these cases and not to use it intermittently. ■

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AngioJet Solent Catheters Combined with Console Abbreviated Statement

CAUTION: *Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.*

INTENDED USE/INDICATIONS FOR USE

The AngioJet SOLENT Proxi & Omni Thrombectomy Sets are intended for use with the AngioJet Ultra Console to break apart and remove thrombus from:

- upper and lower extremity peripheral arteries ≥ 3.0mm in diameter,
- upper extremity peripheral veins ≥ 3.0mm in diameter,
- ileofemoral and lower extremity veins ≥ 3.0mm in diameter,
- A-V access conduits ≥ 3.0mm in diameter and
- for use with the AngioJet Ultra Power Pulse technique for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system.

The AngioJet SOLENT Dista Thrombectomy Set is intended for use with the AngioJet Ultra Console to break apart and remove thrombus from:

- upper and lower extremity peripheral arteries and
- for use with the AngioJet Ultra Power Pulse technique for the control and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system.

The minimum vessel diameter for each Thrombectomy Set model is listed in Table 1 (in the DFU).

CONTRAINDICATIONS

Do not use the catheter/Thrombectomy set in patients:

- Who are contraindicated for endovascular procedures
- In whom the lesion cannot be accessed with the guide wire
- Who cannot tolerate contrast media

WARNINGS

- The Thrombectomy Set has not been evaluated for treatment of pulmonary embolism. There are reports of serious adverse events, including death, associated with cases where the catheter was used in treatment of pulmonary embolism.
- The Thrombectomy Set has not been evaluated for use in the carotid or cerebral vasculature.
- The Thrombectomy Set has not been evaluated for use in the coronary vasculature.
- Operation of the catheter may cause embolization of some thrombus and/or thrombotic particulate debris. Debris embolization may cause distal vessel occlusion, which may further result in hypoperfusion or tissue necrosis.
- Cardiac arrhythmias during catheter operation have been reported in a small number of patients. Cardiac rhythm should be monitored during catheter use and appropriate management, such as temporary pacing, be employed, if needed.
- Use of the catheter may cause a vessel dissection or perforation.
- Do not use the AngioJet Ultra System in patients who have a non-healed injury due to recent mechanical intervention, in the vessel to be treated, to avoid further injury, dissection, or hemorrhage.
- Do not use the Thrombectomy Set in vessels smaller than minimum vessel diameter for each Thrombectomy Set model as listed in Table 1 (in the DFU); such use may increase risk of vessel injury.
- Systemic heparinization is advisable to avoid pericatheterization thrombus and acute rethrombosis. This is in addition to the heparin added to the saline supply bag. Physician discretion with regard to the use of heparin is advised.
- Operation of the AngioJet System causes transient hemolysis which may manifest as hemoglobinuria. Table 1 (in the DFU) lists maximum recommended run times in a flowing blood field and total operating time for each Thrombectomy Set. Evaluate the patient's risk tolerance for hemoglobinemia and related sequelae prior to the procedure. Consider hydration prior to, during, and after the procedure as appropriate to the patient's overall medical condition.
- Large thrombus burdens in peripheral veins and other vessels may result in significant hemoglobinemia which should be monitored to manage possible renal, pancreatic, or other adverse events.
- Monitor thrombotic debris/fluid flow exiting the Thrombectomy Set via the waste tubing during use. If blood is not visible in the waste tubing during AngioJet Ultra System activation, the catheter may be occlusive within the vessel; verify catheter position, vessel diameter and thrombus status. Operation under occlusive conditions may increase risk of vessel injury.
- Obstructing lesions that are difficult to cross with the catheter to access thrombus may be balloon dilated with low pressure (≤ 2 atm). Failure to pre-dilate difficult-to-cross lesions prior to catheter operation may result in vessel injury.
- The potential for pulmonary thromboembolism should be carefully considered when the Thrombectomy Sets are used to break up and remove peripheral venous thrombus.

PRECAUTIONS

- If resistance is felt during the advancement of the Thrombectomy Set to lesion site, do not force or torque the catheter excessively as this may result in deformation of tip components and thereby degrade catheter performance.
- Do not exchange the guide wire. Do not retract the guide wire into the catheter during operation. The guide wire should extend at least 3 cm past the catheter tip at all times. If retraction of the guide wire into the Thrombectomy Set occurs, it may be necessary to remove both the Thrombectomy Set and the guide wire from the patient in order to re-load the catheter over the guide wire. *(Dista only)*
- Do not pull the catheter against abnormal resistance. If increased resistance is felt when removing the catheter, remove the catheter together with the sheath or guide catheter as a unit to prevent possible tip separation.

(Below is Omni, Proxi only)

- Use of a J-tip guide wire is not recommended as it is possible for the tip of the guide wire to exit through a side window on the distal end of the catheter. *(Omni, Proxi only)*
- Hand injection of standard contrast medium may be delivered through the thrombectomy catheter via the manifold port stopcock. Follow the steps to remove air from the catheter when delivering fluid through the catheter stopcock.
- Fluids should be injected only under the direction of a physician and all solutions prepared according the manufacturer instructions.
- The Thrombectomy Set waste lumen is rated for 50psi. Delivering a hand injection of contrast medium with excessive force can create injection pressures greater than 50psi, potentially causing leaks in the waste lumen of the catheter.
- Do not use a power injector to deliver contrast medium through the catheter stopcock. Power injectors can deliver pressures greater than 50psi, potentially causing leaks in the waste lumen of the catheter.
- Some fluids, such as contrast agents, can thicken in the catheter lumen and block proper catheter operation if left static too long. The catheter should be operated to clear the fluid within 15 minutes of injection.

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Console WARNINGS and PRECAUTIONS:

- Use the AngioJet Ultra 5000A Console only with an AngioJet Ultra Thrombectomy Set. This Console will not operate with a previous model pump set and catheter.
- Do not attempt to bypass any of the Console safety features.
- If the catheter is removed from the patient and/or is inoperative, the waste tubing lumen, guide catheter, and sheath should be flushed with sterile, heparinized solution to avoid thrombus formation and maintain lumen patency. Reprime the catheter by submerging the tip in sterile, heparinized solution and operating it for at least 20 seconds before reintroduction to the patient.
- Refer to the individual AngioJet Ultra Thrombectomy *Set Directions for Use* manual for specific warnings and precautions.
- Do not move the collection bag during catheter operation as this may cause a collection bag error.
- Monitor thrombotic debris/fluid flow exiting the catheter through the waste tubing during use. If blood is not visible during console activation, the catheter may be occlusive within the vessel or the outflow lumen may be blocked.
- Ensure adequate patient anticoagulation to prevent thrombus formation in outflow lumen.
- Refer to individual Thrombectomy *Set Directions for Use* manual for specific instructions regarding heparinization of the Thrombectomy Set.
- The Console contains no user-serviceable parts. Refer service to qualified personnel.
- Removal of outer covers may result in electrical shock.
- This device may cause electromagnetic interference with other devices when in use. Do not place Console near sensitive equipment when operating.
- Equipment not suitable for use in the presence of flammable anesthetic mixture with air or with oxygen or nitrous oxide.
- To avoid the risk of electric shock, this equipment must only be connected to a supply mains with protective earth.
- Where the *"Trapping Zone Hazard for Fingers"* symbol is displayed on the console, there exists a risk of trapping or pinching fingers during operation and care must be exercised to avoid injury.
- Do not reposition or push the console from any point other than the handle designed for that purpose. A condition of overbalance or tipping may ensue.
- The AngioJet Ultra 5000A Console should not be used adjacent to or stacked with other equipment, and if adjacent or stacked use is necessary, the AngioJet Ultra Console should be observed to verify normal operation in the configuration in which it will be used.
- Portable and mobile radio frequency (RF) communications equipment can affect MEDICAL ELECTRICAL EQUIPMENT.
- The use of accessories and cables other than those specified, with the exception of accessories and cables sold by Bayer HealthCare as replacement parts for internal components, may result in increased EMISSIONS or decreased IMMUNITY of the Ultra 5000A Console.
- MEDICAL ELECTRICAL EQUIPMENT needs special precautions regarding Electro-Magnetic Compatibility (EMC) and needs to be installed and put into service according to the EMC information provided in the tables provided in the Operator's Manual.

ADVERSE EVENTS

Potential adverse events which may be associated with use of the AngioJet Ultra Thrombectomy System are similar to those associated with other interventional procedures and include, but are not limited to:

- abrupt closure of treated vessel
- acute myocardial infarction
- acute renal failure
- arrhythmia
- bleeding from access site
- cerebrovascular accident
- death
- dissection
- embolization, proximal or distal
- hematoma
- hemolysis
- hemorrhage, requiring transfusion
- hypotension/hypertension
- infection at the access site
- pain
- pancreatitis
- perforation
- pseudoaneurysm
- reactions to contrast medium
- thrombosis/occlusion
- total occlusion of treated vessel
- vascular aneurysm
- vascular spasm
- vessel wall or valve damage

AngioJet ZelanteDVT Thrombectomy Set Abbreviated Statement

CAUTION: *Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.*

INTENDED USE/INDICATIONS FOR USE

The ZelanteDVT Thrombectomy Set is intended for use with the AngioJet Ultra Console to break apart and remove thrombus, including deep vein thrombus (DVT), from:

- Iliofemoral and lower extremity veins ≥ 6.0 mm in diameter and
- Upper extremity peripheral veins ≥ 6.0 mm in diameter.

The ZelanteDVT Thrombectomy Set is also intended for use with the AngioJet Ultra Power Pulse® technique for the controlled and selective infusion of physician specified fluids, including thrombolytic agents, into the peripheral vascular system.

CONTRAINDICATIONS

Do not use the catheter in patients:

- Who are contraindicated for endovascular procedures
- In whom the lesion cannot be accessed with the guidewire
- Who cannot tolerate contrast media

WARNINGS

The ZelanteDVT Thrombectomy Set has not been evaluated for treatment of pulmonary embolism. There are reports of serious adverse events, including death, associated with cases where other thrombectomy catheters were used during treatment of pulmonary embolism.

- The ZelanteDVT Thrombectomy Set has not been evaluated for use in the carotid or cerebral vasculature.
- The ZelanteDVT Thrombectomy Set has not been evaluated for use in the coronary vasculature.
- Operation of the catheter may cause embolization of some thrombus and/or thrombotic particulate debris. Debris embolization may cause distal vessel occlusion, which may further result in hypoperfusion or tissue necrosis.
- Cardiac arrhythmias during catheter operation have been reported in a small number of patients. Cardiac rhythm should be monitored during catheter use and appropriate management, such as temporary pacing, be employed, if needed.
- Use of the catheter may cause a vessel dissection or perforation.
- Do not use the AngioJet Ultra System in patients who have a

non-healed injury due to recent mechanical intervention, in the vessel to be treated, to avoid further injury, dissection, or hemorrhage.
- Do not use the ZelanteDVT Thrombectomy Set in vessels smaller than minimum vessel diameter as listed in Table 1 of the DFU; such use may increase risk of vessel injury.
- Systemic heparinization is advisable to avoid pericatheterization thrombus and acute rethrombosis. This is in addition to the heparin added to the saline supply bag. Physician discretion with regard to the use of heparin is advised.
- The potential for pulmonary thromboembolism should be carefully considered when the ZelanteDVT Thrombectomy Set is used to break up and remove peripheral venous thrombus

PRECAUTIONS
- Systemic heparinization is advisable to avoid pericatheterization thrombus and acute rethrombosis. This is in addition to the heparin added to the saline supply bag. Physician discretion with regard to the use of heparin is advised.
- If resistance is felt during the advancement of the ZelanteDVT Thrombectomy Set to lesion site, do not force or torque the catheter excessively as this may result in deformation of tip components and thereby degrade catheter performance.
- Do not pull the catheter against abnormal resistance. If increased resistance is felt when removing the catheter, remove the catheter together with the sheath as a unit to prevent possible tip separation.

ADVERSE EVENTS

Potential adverse events which may be associated with use of the AngioJet Ultra Thrombectomy System are similar to those associated with other interventional procedures and include, but are not limited to:
- abrupt closure of treated vessel
- acute myocardial infarction
- acute renal failure
- arrhythmia
- bleeding from access site
- cerebrovascular accident
- death
- dissection
- embolization, proximal or distal
- hematoma
- hemolysis
- hemorrhage, requiring transfusion
- hypotension/hypertension
- infection at the access site
- pain
- pancreatitis
- perforation
- pseudoaneurysm
- reactions to contrast medium
- thrombosis/occlusion
- total occlusion of treated vessel
- vascular aneurysm
- vascular spasm
- vessel wall or valve damage

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