

Chronic Venous Occlusion

The medical community is beginning to embrace treatment options for lower-extremity postthrombotic syndrome.

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Venous disorders range from unsightly spider and varicose veins associated with incompetent superficial valves to severe edema, pain, and cutaneous changes secondary to chronic deep vein obstruction. Venous hypertension is the common denominator in this spectrum of signs and symptoms collectively referred to as venous insufficiency. A person may have extremity swelling, pain and discoloration, and ulcers due to valve reflux and/or obstruction (Figure 1). Chronic venous disease is the most common problem in vascular medicine.¹ Careful history, physical examination, and imaging studies provide information for piecing together the puzzle of venous disease and matching the findings to the pathophysiology and etiology of venous hypertension.

CURRENT DATA

The majority of patients with varicosities and stasis changes have problems related to saphenous vein reflux. Postthrombotic syndrome (PTS), including edema, pain, and skin changes, is most often due to combined reflux and obstruction involving deep veins.² PTS can occur when thrombosis is confined to the calf. Obstruction and valve injury in the infrapopliteal veins can produce significant clinical symptoms.³ The frequency of calf deep vein thrombosis (DVT) is, in fact, underappreciated. In nearly 3,000 venograms performed in 2,541 patients during a 10-year period at the Cleveland Clinic, there were 885 documented cases of DVT, and calf vein involvement was seen in 734 (83%) patients.⁴

The principal complaints of a patient with hemodynamically significant residual deep vein obstruction center on a diminished quality of life and disability related to having a heavy and/or painful limb. Obstructive venous problems can be lifelong, leading to limb conditions that cause substantial morbidity, lost workdays, early retirement, and the

need for chronic medical care. Symptomatic venous obstruction can significantly decrease quality of life during prime working years, or as individuals approach retirement. Venous insufficiency increases with age, so as baby-boomers enter their fifth, sixth, and seventh decades of life, the prevalence of venous disorders will increase, resulting in a greater medical-cost burden for treatment of leg swelling, leg pain, thrombophlebitis, and stasis ulcers.

In 1992, Hume estimated that 3% of the Medicare population has a venous stasis ulcer.⁵ Approximately one person in 1,000 is estimated, at any point in time, to have an unhealed ulcer. With the population of the US approaching 290 million people, more than 2 million persons among the Medicare age group have a healed or unhealed ulcer caused by venous disease. Many of the patients we treat are relatively young; they are in their 20s and 30s when they develop DVT. Data (1999-2000) from a major US insurance company show 5.2 claims (per 1,000 insured)



Figure 1. Signs of venous hypertension, hyperpigmentation and telangiectasia seen at the medial malleolar level.

indicate venous insufficiency. This is in addition to 2.1 of 1,000 representing the primary diagnoses of thromboembolism (personal communication. Mutual of Omaha, August 2000).

A recent epidemiologic study was launched in 1994 to study the prevalence of venous diseases in a homogenous population with a low level of immigration or migration for the past 30 years.⁶ In 1996, it was shown that 8.6% of the population (mean age, 46.3 years; range, 8-94 years) had a clinically relevant venous problem. In 3%, the problem was severe, meaning they had been or were under medical treatment or had required hospital admission. In 2.8%, the problem was documented objectively, but remained subclinical. The average cost per patient for a year's treatment was € 850, including hospital costs, lost workdays, and medical products. It is emphasized that, considering that venous diseases are chronic in nature, the community costs make these diseases a major health-care problem. The authors go on to say, "Inefficiency, lack of prevention and differences of standards probably double the costs of venous diseases."⁶

The symptoms of PTS get worse during the day because of gravity and progress over time. Standard compression therapy may not adequately address the edema and discomfort that begin shortly after the patient gets out of bed each day (Figure 2). Motivated patients find themselves struggling to stay at work or do any extra activities with their families. Ultimately, they face the issue of actually maintaining their employment as they exhaust their sick days and search for time and opportunities to elevate their leg to relieve the pressure. Patients with PTS are commonly told that they must learn to live with the condition because there is no treatment, other than compression, for chronic DVT. Patients severely disabled by nonmalignant ilio caval occlusion have limited surgical options. Patency results of long bypass grafts for large vein obstruction are inconsistent, even when assisted with an arteriovenous fistula.⁷ Not infrequently, the graft will fail due to intimal hyperplasia at the anastomosis. Angioplasty and stenting provide endovascular solutions to assist patency of surgically treated chronic central venous obstruction.⁸

Percutaneous endovascular reconstruction of lower-extremity chronic deep vein occlusion has been shown to be feasible with acceptable long-term patency. O'Sullivan et al reported 93.9% 1-year patency in 20 patients treated for chronic left iliac obstruction.⁹ Neglen reported similar



Figure 2. Postthrombotic limb, left-lower-extremity edema, and distal calf hyperpigmentation. Progressive heaviness and discomfort accumulate during the day and are not controlled with compression stocking.

experience in a larger study that included 2-year follow-up of endovascular treatment of chronic venous obstruction causing PTS.¹⁰ Among 139 patients (mean age, 47 years) with documented venous outflow obstruction, 78 patients had post-thrombotic disease, whereas 61 had iliac vein compression without thrombotic complications. The primary, primary-assisted, and secondary cumulative patency rates were 52%, 88%, and 90% for PTS patients compared to 60%, 100%, and 100% for patients with iliac compression without DVT.

We are particularly interested in the long-term patency of stents placed in young adults. When the thrombus is extensive and does not resolve, a young, active individual is left with an unwelcome disability that may totally alter quality of life, relationships, and career. For example, one patient was a 21-year-old man who developed bilateral iliofemoral DVT. In July

2000, the patient was hospitalized due to left leg DVT. He was hospitalized again in July 2001 due to recurrent DVT. By April 2002, he had developed a left stasis ulcer. In July 2002, he was hospitalized for acute right leg DVT and was unable to return to work. In 1981, as a 2-month-old preemie, he had numerous central lines placed. Twenty-one years later, he experienced bilateral DVT that led to PTS. A venogram revealed infrarenal caval occlusion and chronic iliofemoral thrombosis (Figure 3). He was treated with endovenous reconstruction using 17 self-expanding stents. He remained asymptomatic at 18 months. He is an example of the numerous patients who develop symptomatic venous occlusion associated with central venous catheters.¹¹

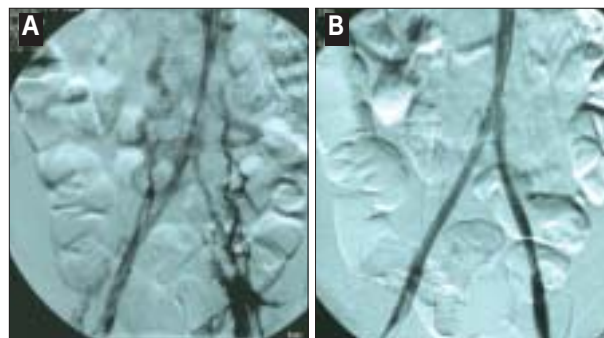


Figure 3. Pre- and postvenogram images of partially reopened iliofemoral channels after 72 hours of catheter-directed lytic therapy in a 21-year-old man. The patient had chronic IVC occlusion secondary to central line placement as an infant.

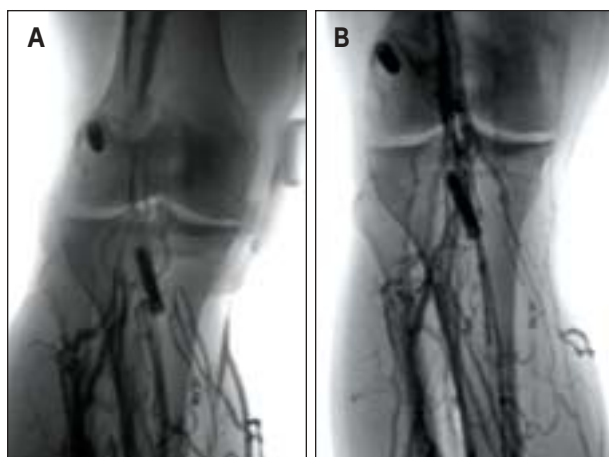


Figure 4. Pre- and postthrombolysis venogram of right calf and popliteal segment in a 52-year-old man with disability related to pain and edema. The symptoms persisted 2 years after DVT complicated knee surgery. He responded well to flow-directed urokinase therapy that re-established continuity of flow from the calf to the femoral vein.

Subsequently, we reviewed 28 patients aged 12 years to 30 years (mean age, 19 years, 4 months) treated for lower-extremity thrombosis. Chronic conditions were revealed in nearly half of those presenting with acute DVT. Five patients were referred with PTS with a mean duration of symptoms of 12.6 months. Follow-up ranged between 7 months and 9 years (mean, 4.5 years). Primary stent patency was 72% (23 of 32) and assisted patency was 87.5% (28 of 32). The collective endovascular experience suggests that endovascular reconstruction of chronic venous occlusion can be done with low morbidity and good clinical results that endure.¹²

MORE NEEDS TO BE DONE

Stenting of chronic venous occlusion to treat disabling PTS is a seemingly viable option. Why is it not offered to more patients with this condition? Physicians know that thrombolytic therapy involves expense and risks that are difficult to weigh against the probability of an individual developing PTS. Most physicians think that catheter-directed thrombolysis is only a tool for acute DVT and, therefore, not an option when thrombus is months or years old. While technically more challenging, endovascular therapy (thrombolysis, angioplasty, and stenting) can be used to effectively and safely re-establish flow in chronic, totally occluded axial veins. This is a promising therapeutic option for selected patients with disabling PTS.

The procedure is demanding because it involves passing wires and catheters through old, organized thrombus. Technical skills, honed in hours of arterial work, prepare

the physician who wishes to treat chronic venous disease. Thrombolysis is used to soften the old thrombus when it is not possible to pass a wire through the obstruction to the inferior vena cava. An overnight lytic infusion of what I call “low-dose, high-volume” is employed. In our institution, we now use urokinase at 1,000 IU/mL and infuse 50-100 mL/hour. We generally approach from a distal site and prefer a popliteal vein access just above the crease of the knee. Others achieve access through superficial routes, such as the lesser saphenous, and some will use the distal tibial entry point. An ultrasound-guided, single-wall puncture is ideal to prevent arterial injury and hematoma. A diagnostic ascending venogram accompanies all procedures and provides an initial understanding of the flow pattern caused by the obstruction.

The challenge is to design an endovascular therapy that effectively improves flow at all levels. If calf vein thrombosis prevents tibial flow, we fluoroscopically position tourniquet discs to compress the greater saphenous vein at the ankle and the knee. This blocks the path of least resistance (ie, the saphenous vein) and diverts the lytic agent into the tibioperoneal veins. Increasing venous flow capacity in the calf is an important concept for optimizing deep system flow and clinical results. The venographic image may remain abnormal, but the improvement in contrast clearance, upon injection from the pedal site, will indicate better flow as treatment succeeds. Poor flow into the popliteal vein, via the gastrocnemius and soleal veins, can result in persistent calf pain and edema, as well as decreased patency of reopened or stented iliofemoral segments. Re-establishing continuity of flow from the foot to the thigh can reduce pain and edema related to popliteal and calf vein obstruction. This was well demonstrated in a



Figure 5. An IVUS image from a 20-MHz probe (Boston Scientific Corporation, Natick, MA) that shows anterior-posterior luminal narrowing in the left common iliac vein consistent with Mayn-Thurner syndrome.

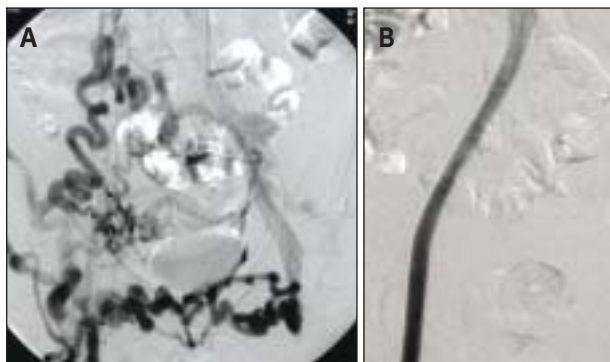


Figure 6. A pelvic venogram (prone) showing before (A) and after (B) endovascular intervention to treat severe right-lower-extremity PTS in a 43-year-old woman who had recurrent DVT (twice) and a 5-year history of postthrombotic syndrome.

patient who had popliteal DVT after knee surgery. Figure 4 shows the pre- and postthrombolysis images. This patient was at risk of losing his job and pension due to inability to work a full shift. After flow-directed urokinase at 100,000 IU/hour for 60 hours, using flow-directed technique of intermittent saphenous compression, the patient was improved clinically. The change in the venogram, albeit notable, is not spectacular. But, the improved venous physiology resulted in decreased pain and swelling and a big change in quality of life.¹³

Upon traversing the obstruction with a wire, it may be necessary to dilate the track with a small-diameter balloon to advance a catheter. Once a 4-F or 5-F catheter can be advanced through the occlusion, a working wire can be placed to support the serial balloon dilatations that precede stent placement. I advocate expanding the chronically occluded vein before deploying self-expanding stents. Intravascular ultrasound (IVUS) is an excellent tool for evaluating the degree of anterior-posterior compression in the common iliac segment (Figure 5). In patients in whom we place multiple stents, a PTT between 50-80 seconds is maintained until the INR is >2.0 . A single stent in the iliac vein, without thrombosis in the distal veins, is not treated with anticoagulation. Clopidogrel (75 mg per day) is started prior to stenting. The popliteal sheath is removed with the patient in the prone position and without altering the heparin infusion. We keep patients at bed rest for 24 hours after the sheath is removed because, in our experience, more hematomas occur with earlier ambulation. Patients are followed with ultrasound to document patency.

CASES

Case No. 1

A recent case involved a 43-year-old woman with a 9-year history of PTS. Her left leg pain and edema were caus-

ing progressive inability to perform her job as a nursing assistant. She was at risk of losing her job and health insurance. She was positive for heterozygous Factor V Leiden mutation and had two hospitalizations for left leg DVT since the initial episode in 1995. She was referred from the hematologist for evaluation and possible endovascular therapy. Her physical exam revealed dependent discoloration, focal hyperpigmentation, and telangiectasias at the medial malleolus for CEAP IV classification. She was unable to complete an 8-hour shift despite class II compression stockings and used daily pain medication and leg elevation. Her reconstruction took a total of three visits to the angiosuite and 4.5 hours of procedure time. The before and after venogram of the pelvis show the extent of collateral flow that still failed to alleviate the venous hypertension caused by the thrombotic occlusion of the iliac and common femoral segments (Figure 6). The pain and edema have resolved significantly after stent placement and she resumed full-time activities within 1 week of discharge after achieving a therapeutic warfarin level (INR >2.0).

Case No. 2

Another case involved a 38-year-old man who traveled a lot for work. Although his history finally revealed a nonevaluated incident of left leg swelling that occurred 7 months prior to the patient's hospitalization, he had no documented knowledge of prior DVT. His massive left leg thrombosis was poorly compensated by small superficial veins. After 2 months of heparin and warfarin, including an interval discharge that failed, the patient was referred for evaluation and treatment. The patient underwent flow and catheter-directed lytic administration via the foot and popliteal access points. A retrograde jugular placement of a catheter was used to treat thrombus sitting below the popliteal sheath. He ultimately benefited from placement



Figure 7. Images of a patient before (A) and after (B) 1 week of therapy for a massive chronic left leg venous obstruction extending from the calf to the IVC.

of seven overlapping stents extending from the inferior vena cava to the mid thigh (Figure 7).

We have entered an era in medicine and surgery in which minimally invasive therapies are providing desired results with less morbidity than conventional therapy. This is seen in the areas of cardiac intervention, laparoscopic surgery, and treatment of arterial vascular disease, such as aortic aneurysm and carotid stenosis. Venous disorders have been underdiagnosed and undertreated for many years. We now have at hand better ways to evaluate and treat venous disease. Ultrasound makes screening noninvasive and painless. Thrombolytic therapy can effectively and rapidly dissolve acute thrombus (0-14 days) with low morbidity and mortality and thereby prevent damage that leads to PTS.¹⁴

Among persons diagnosed with DVT, it is estimated that more than 80% of those treated with standard heparin therapy alone will develop a chronic condition of venous insufficiency, with nearly 50% characterized by constant leg pain and/or swelling.² It has been well demonstrated that standard heparin therapy for multisegment, lower-extremity thrombosis leaves most individuals with unwanted clinical sequelae. When patients suffer from the effects of residual obstruction and damaged valves, endovascular intervention, rather than bypass surgery, has been shown to give effective and lasting improvement.¹⁵⁻¹⁷ It is disappointing, therefore, to read the conservative stance taken regarding prevention and treatment of PTS in a recent article by Kahn and Ginsberg.¹⁸ They endorse compression therapy while noting the lack of level 1 data regarding thrombolysis in the treatment of DVT. Longitudinal clinical studies are difficult. We showed a significant decrease in postthrombotic pain in patients with acute DVT treated with urokinase compared to similar patients treated with heparin alone. The clinical improvement in postthrombotic pain was documented in the 10-year follow-up study.¹⁹ Further studies are needed to corroborate the decrease in PTS after early thrombolytic therapy.

CONCLUSION

The medical community has been slow to address the seriousness and immense morbidity and cost of venous disease. Venous conditions last a lifetime, and slowly manifest their debilitating effect. Although the risk of pulmonary embolism is appreciated as life-threatening, how often do physicians consider the life-altering morbidity and cost of leaving a limb filled with thrombus that may cause PTS? For extensive multisegmental obstructive thrombosis, is anticoagulation for 3 to 6 months sufficient? How many times will patients return for medical care related to the first event? How do we

better predict who will fail conservative therapy?

We are now beginning to see an awakening in the medical community to the seriousness of venous disease.^{20,21} Long recognized by our European colleagues as a major health issue, US medical communities are now starting to realize that treating peripheral vascular disease means including venous disorders alongside arteriosclerosis because it is the most common problem in vascular medicine. With the advent of minimally invasive therapies with durable clinical results, we have the opportunity to intervene and interrupt a disease process that has defied clinicians for centuries.²² ■

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1. Ricotta JJ, Dalsing MC, Ouriel K, et al. Research and clinical issues in chronic venous disease. *Cardiovasc Surg.* 1997;5:343-349.
2. Johnson BF, Manzo RA, Bergelin MS, et al. Relationship between changes in the deep venous system and the development of the post-thrombotic syndrome after an acute episode of lower limb deep vein thrombosis: a one- to six-year follow-up. *J Vasc Surg.* 1995;21:307-313.
3. Saarinen J, Domonyi K, Rainer Z, et al. Postthrombotic syndrome after isolated deep venous thrombosis: the role of popliteal reflux. *J Vasc Surg.* 2002;36:1-6.
4. Ouriel K, Green R, Greenberg R, et al. The anatomy of deep vein thrombosis of the lower extremity. *J Vasc Surg.* 2000;31:895-900.
5. Hume M. Venous ulcers, the vascular surgeon, and the Medicare budget. *J Vasc Surg.* 1992;16:671-673.
6. Belcaro G, Nicolaidis AN, Stansby G. The venous clinic: diagnosis, prevention, investigations, conservative and medical treatment. Sclerotherapy and Surgery. Imperial College Press, London: 1998.
7. Glowiczki P, Pairero PC, Toomey BJ, et al. Reconstruction of large veins for non-malignant venous occlusive disease. *J Vasc Surg.* 1992;16:750-761.
8. Kalra M, Glowiczki P, Andrews J, et al. Open surgical and endovascular treatment of superior vena cava syndrome caused by non-malignant disease. *J Vasc Surg.* 2003;38:215-223.
9. O'Sullivan GJ, Semba CP, Bittner CA, et al. Endovascular management of iliac vein compression (May-Thurner) syndrome. *J Vasc Intervent Radiol.* 2000;11:823-836.
10. Neglén P, Raju S. Balloon dilation and stenting of chronic iliac vein obstruction: technical aspects and early clinical outcome. *J Endovasc Ther.* 2000;7:79-91.
11. Hausler M, Hubbner D, Dehhaas T, et al. Long term complications of inferior vena cava thrombosis. *Arch Dis Child.* 2001;85:228-233.
12. Thorpe P, Osse F. Endovascular therapy for relief of symptomatic lower extremity venous obstruction in young adults and juveniles. Presented at The XVI International Congress for Endovascular Interventions. Phoenix, AZ; February 9, 2004.
13. Thorpe PE. The role of flow-directed thrombolytic therapy for lower extremity thrombosis: evaluating and treating the entire limb. *J Endovasc Ther.* 2000;7:1-37.
14. Grunwald MR, Hofmann LV. Comparison of urokinase, alteplase, and reteplase for catheter-directed thrombolysis of deep venous thrombosis. *J Vasc Intervent Radiol.* 2004;15:347-352.
15. Thorpe PE, Osse FJ, Dang HP. Endovascular reconstruction for chronic iliac vein and inferior vena cava obstruction. In: Glowiczki P, Yao JST Eds. Handbook of Venous Disorders: Guidelines of the American Venous Forum, 2nd Ed. Arnold, a Member of the Hodder Headline Group, London: 2001; pp. 347-361.
16. Nazarian GK, Austin WT, Wegryn AS. Venous recanalization by metallic stents after failure of balloon angioplasty or surgery: four-year experience. *Cardiovasc Interv Radiol.* 1996;19:227-233.
17. Neglén P, Thrasher TL, Raju S. Venous outflow obstruction: an underestimated contributor to chronic venous disease. *J Vasc Surg.* 2003;38:879-885.
18. Kahn SR, Ginsberg JS. Relationship between deep venous thrombosis and the postthrombotic syndrome. *Arch Intern Med.* 2004;164:17-26.
19. Thorpe P, Osse F. Thrombolytic therapy versus anticoagulation for treatment of deep vein thrombosis: ten-year experience. Presented at the 29th Annual SIR Meeting, Phoenix, AZ; March, 25, 2004.
20. Bergan JJ. Prospects for minimal invasion in venous disease. *Vasc Surg.* 1999;33:247-250.
21. Wakefield TW. Treatment options for venous thrombosis: invited review. *J Vasc Surg.* 2000;31:613-620.
22. Bergan JJ, Kumins NH, Owens EL, et al. Surgical and endovascular treatment of lower extremity venous insufficiency. *J Vasc Intervent Radiol.* 2002;13:563-568.