Management of Chronic Deep Vein Thrombosis in Women

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Abstract

Keywords

- Chronic Deep Vein Thrombosis
- IVC stenting
- venous stasis
- interventional radiology

Chronic deep vein thrombosis (DVT) affects hundreds of thousands of women in the United States. Chronic DVT can lead to pain, edema, venous ulcers, and varicosities. While there are limited data regarding the management of chronic DVT, several interventional radiology groups aggressively treat chronic DVT to aid patient symptom resolution. Recanalization of occluded veins and venous stenting re-establishes deep vein flow and decreases venous hypertension.

Objectives: Upon completion of this article, the reader will be able to evaluate women with chronic DVT, identify patients who warrant treatment, and develop a treatment strategy for chronic DVT.

While acute deep vein thrombosis (DVT) is more common in men, with a relative risk of 1.2 to 1.4, hundreds of thousands of women are affected by acute and chronic DVT each year.¹ Additionally, certain groups of women are at increased risk for DVT over their peers. Oral contraceptives (OCPs) are known to increase risk of DVT two to three times.¹ Pregnancy also increases risk of DVT approximately five times.² Women with thrombophilia disorders are at very high risk: for example, women with both factor V Leiden and using OCP are at a 34-fold increased risk for DVT.³

Given the prevalence of DVT in women, many of who will have delayed diagnosis and treatment, many women encounter the sequelae of chronic DVT. Chronic DVT leads to many long-term complications, including lower extremity pain and edema, and increased venous pressures can cause skin eczema, hyperpigmentation, ulcers, and venous varicosities⁴; pain and ulcers can be lifestyle limiting.

While there is controversy regarding the best treatment and course of action in these women, many interventional

radiologists advocate aggressive recanalization of chronic iliac and inferior vena cava (IVC) clot. The ATTRACT trial provides a randomized control trial for acute DVT, but does not address the chronic DVT scenario.⁵

Single-center chronic DVT treatment results suggest high patency rates after intervention and symptomatic improvement.^{4,6–13} Several of these studies are performed predominantly in women.^{7,9}

Clinical Evaluation

Women with suspected DVT are evaluated as outpatients in the interventional radiology clinic. Pertinent clinical history includes duration of symptoms, inciting events, and treatments. At the University of Utah, a mid-size academic medical center serving 10% of the geography of the United States, interventionalists inquire into prior thrombosis events, bleeding history, and any contraindication to anticoagulation (e.g., prior stroke, surgery, intracranial hemorrhage, and bleeding). Medication and drug allergies are documented, as well as contrast allergies and renal insufficiency. Family history for DVT is important to evaluate. In addition, physicians usually have the internal medicine thrombosis clinic evaluate the patient for thrombophilia, including protein C, protein S, antithrombin III deficiency,

lupus anticoagulant, anticardiolipin antibody, factor V Leiden mutation, factor VII activity, factor XI activity, and homocysteine levels.

Physical examination includes evaluation of the bilateral legs and abdomen. Photographs are often obtained and uploaded in the patient's record. Legs should be evaluated for edema (with diameter measurements), skin changes including hyperpigmentation and lipodermatosclerosis, and skin ulcerations (—Fig. 1). The author calculates Clinical–Etiology–Anatomy–Pathophysiology (CEAP) classification score and Venous Clinical Severity Scores (VCSS)¹⁴ and documents these in the medical record.

Imaging evaluation starts with lower extremity ultrasound. While most ultrasound reports will comment on the presence of thrombus and reflux, some of the additional signs of chronic thrombus usually require the interventional radiologist to study the images or perform targeted examination in the office. The American College of Radiology (ACR) provides guidelines for lower extremity ultrasound. The examination should include compression, color and spectral Doppler, and augmentation.¹⁵ Thrombosis is diagnosed by luminal filling defect on gray-scale images, vein distention, absence of color Doppler, and loss of phasicity and augmentation.¹⁵ Acute DVT has a hypoechoic appearance and the vein is usually distended. Chronic DVT remains noncompressible, and the vein becomes narrow and shows wall thickening and synechiae. There are regions of recanalization and color flow with echogenic peripheral thrombus.¹⁶

To evaluate the IVC and pelvic veins, computed tomography venography (CTV) or magnetic resonance venography (MRV) is performed. MRV is preferred at some hospitals and can provide high-quality images without radiation. To reduce pelvic radiation, the author prefers MRV in young females on

OCP or pregnancy. Magnetic resonance direct thrombus imaging (MRDTI) also has the ability to differentiate acute from chronic thrombus and delineate the extent of acute thrombus.¹⁶ CTV is readily available, fast to obtain, and provides high resolution of the veins and abdominal organs. CTV images are acquired by administering approximately 150 mL of intravenous contrast and imaging at approximately 80 to 100 seconds after injection.¹⁶ CTV also evaluates extrinsic compression on the veins such as masses.

Treatment

While there are no large randomized trials involving recanalization in chronic DVT, there are several reports showing improved patient symptoms, resolution of venous ulcers, and sustained venous patency.^{4,7,9,10,17,18} The author has also noted vastly improved symptoms after venous recanalization, leading the author's group to aggressively treat patients with CEAP ≥ 3 .

To perform the procedure, patients are scheduled with anesthesia as recanalization can be a prolonged procedure and patient discomfort can impact success. Prolonged venoplasty of scarred veins can also be very painful to the patient. For these reasons, the author has found it best to perform the case under monitored anesthesia care or general anesthesia. Anticoagulation medicines are maintained during the procedure, usually enoxaparin or intravenous heparin.

Most patients are positioned supine, and venous access is obtained either at the mid-thigh femoral vein or posterior tibial vein under ultrasound guidance. Tibial thrombus requires access of the posterior tibial vein. In this instance, since the tibial veins are prone to vasospasm, a single wall puncture should be obtained. Mid femoral vein access allows for full

Fig. 1 A 42-year-old woman with a history of cervical cancer. She developed right lower extremity deep vein thrombus (DVT) and pulmonary embolism. She also had a history of venous insufficiency and reflux. She was treated with enoxaparin for 3 months. Fifteen months after the right leg DVT, she developed a venous stasis ulcer. She had been treated with compression stockings, but could not wear the stockings for extended times due to severe pain over the ulcer. Ultrasound shows venous wall thickening and severe greater saphenous vein reflux. (a) Patient's posteromedial calf varicose veins (black arrow). (b) Venous ulcer (white arrows). (Images from Ziga Cizman, MD.)

evaluation of the common femoral vein and catheter pushability in the iliac veins. The author uses a 21-G micropuncture for access of the tibial vein or femoral vein. The tip of the needle should be confirmed in the vein and there should be blood return. Care should be taken while placing the 0.018-inch wire, as needle tip location outside of the lumen also results in venospasm. The 21-G needle is exchanged for a 5-Fr micropuncture coaxial catheter system, after which the micropuncture catheter is exchanged for a 5-Fr sheath. The author prefers to place a 13-cm sheath initially for venography (Performer Introducer; Cook Medical, Bloomington, IN). As the author usually places a long 5-Fr sheath (Flexor Ansel Guiding Sheath, Cook Medical) for support while crossing venous occlusions, the 13-cm sheath is exchanged after venography.

Venography typically shows the main channel as a thin line (termed a "string" sign).^{13,19} The vein is crossed using a 4- or 5-Fr catheter in combination with a hydrophilic wire. A braided catheter, such as the Cook CXI (Cook Medical), and a stiff Glidewire or Glidewire Advantage (Terumo Medical, Somerset, NJ) are used. The wire is directed through the center of the vein using a spinning motion to avoid collaterals or dissection. The catheter and 5-Fr sheath track near the tip of the wire to provide stability to the system. The wire should not be allowed to form a loop, as this can lead to dissection or selecting a collateral rather than the occluded vein.

Slow progress is made through the iliac veins and into the IVC. The catheter is tracked to the nonoccluded IVC; venography is performed to confirm intraluminal catheter location. Frequently, jugular access is needed to obtain through-and-through access from the IVC to the superior vena cava. The wire can be snared and pulled through the jugular vein, establishing through-through access. A long 8-Fr sheath is used in the jugular vein to place a snare (ONE Snare, Merit Medical, South Jordan, UT) and pull the wire through the sheath. Pullback venogram is performed using the sheath to confirm the venous course. The author has a low threshold to use intravascular ultrasound (IVUS; Volcano, Philips Healthcare, Eindhoven, the Netherlands) to evaluate the location of the access with respect to the iliac arteries and renal veins. The vein often needs to be dilated with a 4-mm balloon to allow the IVUS to pass. Through-through access enables balloons and sheaths to be advanced even through very tight stenoses, as tension can be placed on each side of the wire.

If no channel can be found through the IVC using the hydrophilic wire and braided sheath, some operators describe success in performing thrombolysis from the section of recanalized vein. An Ekosonic Endovascular System catheter (EKOS; BTG Interventional Medicine, West Conshohocken, PA) or Cragg-McNamara catheter (Covidien, Plymouth, MN) is placed in the most cephalad-confirmed portion of the IVC. Thrombolysis is performed overnight with Alteplase (Genentech, San Francisco, CA) infusing at 1.0 mg/hour.

The chronically thrombosed vein is then treated with venoplasty. The length of the vein is sequentially dilated, from the access to the IVC. Venoplasty is started with a 6-mm balloon; long balloons are used to minimize venoplasty zones (Mustang 6 × 18 cm; Boston Scientific, Marlborough,

MA). The balloon is inflated for at least 30 seconds at each segment. Venoplasty is repeated along the length of the vein using an 8-mm balloon, again for sustained inflation of at least 30 seconds. Venoplasty is continued using a 10-mm balloon from the femoral vein and extending into the IVC. Progressively larger balloons are used at the iliac veins and IVC. Step-wise dilation is performed until the common femoral vein is dilated to 12 mm, external iliac veins dilated to 14 mm, common iliac veins dilated to 16 mm, and IVC to 20 mm (Atlas balloons; Bard Medical, Tempe, AZ). Repeat venography is then performed. If there is good flow through the tibial veins and femoral veins but not the iliac veins and IVC, stenting is performed of the central veins, which is often necessary. If there is significant irregularity of the tibial and femoral veins, thrombolysis with Alteplase is performed overnight. While Garcia and Dumantepe et al have reported separate studies on using EKOS for chronic DVT, the author typically uses a Cragg-McNamara catheter for overnight thrombolysis.^{17,20} The typical total dose is 1 mg/hour; if bilateral thrombolysis is performed (and it usually is required), 0.5 mg/hour is used via each catheter placed through the bilateral venous access.

Venous stenting is frequently needed of the IVC and iliac veins to maintain flow and venous patency. Venous stents should be oversized approximately 20%. The author prefers to use Wallstents (Boston Scientific, Marlborough, MA) in the

Fig. 2 A 15-year-old female with a history of right leg deep vein thrombosis (DVT) that occurred after a bunionectomy surgery 1 year prior. She was treated with 3 months of enoxaparin. Her symptoms improved, but she still noticed right leg edema and early right leg fatigue during sports. She presented 1 year after the previous DVT with left leg swelling and pain. Initial venogram showed IVC and iliac vein obstruction with minimal flow. The superficial and common femoral veins were patent. The main-channel IVC could not be determined, and lysis was performed through the bilateral iliac veins with the catheter tip at the confluence of the iliac veins with 0.5 g/hour alteplase.

IVC, of at least 20 mm in diameter. While the author has previously used kissing Wallstents at the iliac confluence, recently kissing Gianturco Z-stents (Cook Medical) at the confluence are used, as described by Raju.²¹ Such stents are also oversized by 20%.^{10,21} The iliac veins are then stented with 16-mm Wallstents. The stent is deployed above the inguinal ligament, maintaining the venous patency and inflow that is necessary for long-term success. Neglén et al demonstrated high long-term patency rates for Wallstents placed across the inguinal ligament and common femoral vein.²²

Patients are usually observed overnight and placed on intravenous heparin, with a goal partial thromboplastin time (PTT) titrated between 60 and 90 seconds. Patients are then started on enoxaparin at 1 mg/kg every 12 hours and discharged on enoxaparin.

► **Figs. 2–4** represent standard technique as performed by the author for venous lysis and stenting.

Inferior Vena Cava Filters

Frequently, a previously placed IVC filter contributes to patient's caval thrombosis. The first plan in these patients is to attempt to remove the IVC filter, which is usually successful, but may require advanced techniques. While details on advanced filter retrieval are beyond the scope of this review, details on IVC filter removal and management

are found in the *Seminars of Interventional Radiology* Issue 2 from 2016.

The author believes it is safe to stent across a filter to allow the filter to be excluded from the recanalized venous channel. Neglén et al reported a series where they placed stents over incorporated IVC filters in 25 patients.²³ They achieved technical success in all patients but one, who had a Mobin-Udin filter. Wallstents were most commonly used to exclude the filter. These authors demonstrated a slightly higher, but not statistically significant, stent occlusion rate compared with patients in whom no filter was ever placed.

Follow-up

Patients are discharged on enoxaparin and return for follow-up in approximately 2 to 3 weeks. Patients are evaluated clinically for symptoms—if they show no improvement in swelling, venous ultrasound is performed. Repeat venography and venoplasty or thrombolysis may be required. If the patient has no thrombosis on ultrasound, but remains symptomatic, he or she is continued on enoxaparin. If edema has improved, patients are usually transitioned to either Xarelto or warfarin. The author works with the thrombosis center to determine the appropriate anticoagulation regimen. Women with obesity and insurance difficulties are usually treated with warfarin. Compression stockings are continued for at least 3 months. Patients are asked to return

Fig. 3 A 15-year-old female after venous lysis. Same patient as Fig 2. Imaging post overnight alteplase thrombolysis. At this time, the main channel of the IVC was crossed, from jugular access as well as femoral access. (a) Venography shows occlusion of the IVC extending to the suprarenal IVC. Plasty was performed using 20-mm atlas balloons in the IVC and 14-mm atlas balloons in the iliac veins (Bard Medical, Tempe, AZ). (b) Venography shows that the IVC and common iliac veins remain occluded despite venoplasty and overnight venous lysis.

Fig. 4 A 15-year-old female after venous stenting. Follow-up venograms after stenting of the IVC and iliac veins. A 20-mm Wallstent was deployed in the IVC. The stent was dilated to 20 mm. Stent was placed via the jugular access. The left iliac vein wire was introduced through the stent, using a spinning pigtail catheter to confirm that the wire was through the stent and not through interstices. Kissing 16-mm Wallstents were placed at the iliac vein confluence. Stents were extended to the level of the external iliac veins that showed normal flow without irregularity or stenosis. Patient was started on enoxaparin 1 mg/kg.

for evaluation at 3 months, 6 months, and 1 year. Life-long anticoagulation is maintained if patients have thrombophilia, unprovoked DVT, or suprarenal stenting.

Outcomes

As previously stated, no randomized control trials exist for chronic DVT. There are several single-center reports for chronic DVT. Hartung et al reported on 89 patients, 72 of who were women, followed up for a mean of 38 months.⁹ Primary patency was 78% and secondary patency was 90%. Grilli et al showed outcomes of chronic DVT management with a mean follow-up of 2 years and 7 months¹⁷; 93% reported significant symptom improvement. Patency was 88% at 6 months, 79% at 1 year, and 58% at 24 months. Friedrich De Wolf et al reported on 63 patients (71% women) with chronic DVT and reconstruction.⁷ Symptom relief was seen in 81% of patients in this group. Primary patency was 74.3% at 12 months and secondary patency was 96.1%. Murphy reports on 71 patients with chronic DVT recanalization (42% women).¹⁰ Their group had an 85% technical success, including two patients who had surgically placed IVC clips. Mean follow-up was 48 months. All patients in whom they could recanalize the IVC showed symptom improvement. Active ulcers healed in 17 out of 18 with venous stasis ulcers.

Conclusion

Chronic DVT is a common disorder in women, resulting in severe life-long symptoms. While randomized controlled

trials are needed for this condition, available studies show great patient outcomes and improved symptoms when treated with prolonged venoplasty and stenting.

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