Postprocedural Management After Endovascular DVT Therapy

Tips for providing diligent and tailored follow-up care to optimize clinical outcomes after endovascular intervention.

BY SURESH VEDANTHAM, MD

In current practice, patients who are highly symptomatic with acute or chronic lower extremity deep vein thrombosis (DVT) are often managed with some form of catheter-directed thrombolysis (CDT) or recanalization. During the last 5 to 10 years, endovascular methods have been substantially refined, such that a patient's likelihood of undergoing a safe procedure that produces the desired initial clinical improvement is now quite strong. However, endovascular DVT therapy is provided over a brief period (1–2 days at most) that constitutes a tiny fraction of the patient's entire life, during which, he or she will remain at risk for recurrent thrombosis. Although CDT studies continue to improve in methodological rigor, the optimal strategies with which to maintain patency of the venous system postintervention, and to retain and optimize the accompanying clinical improvement, have not been defined.[1,2]

As such, postintervention care represents more "art" than "science," with local context and personal experiences playing a major role in shaping any practitioner's approach. Although other reasonable methods certainly exist, in this article, one approach to thinking about postintervention DVT care is presented. Because many details are flexible, it is very important for endovascular practitioners to practice longitudinal follow-up on all treated patients to ensure that they are well managed, understand the signs and symptoms of possible recurrence, and notify the physician if their symptoms or clinical condition changes.

THE IMPORTANCE OF MAINTAINING VENOUS PATENCY

The process of restoring flow to the venous system involves substantial patient risk, physician/provider work effort, and health care system resources, so ensuring a durable clinical benefit to the patient is paramount. Maintaining venous patency is critical to achieving a favorable long-term outcome. Recurrent DVT has a strong association with postthrombotic syndrome (PTS), presumably because it further impairs the structural and functional status of the deep veins and also reactivates the inflammatory response to thrombosis.[3] In DVT patients treated with anticoagulation alone and those treated with additional CDT, quantitative studies have shown that the volume of residual thrombus posttreatment correlates with the future risk of recurrent venous thromboembolism (VTE) and/or PTS.[4-7]

A loss of venous flow patency within 1 to 3 months after CDT may be more common than is often discussed, occurring in perhaps 20% of patients who have undergone CDT in nonrandomized studies.[8] This may partly reflect incomplete thrombus removal and the fact that the population of DVT patients who are referred for CDT tends to be skewed toward highly thrombogenic individuals who did not initially respond well to anticoagulation alone. Nevertheless, that is the real-world patient cohort that we are dealing with, so strong active efforts must be made to maintain patency over time. Whichever approach is chosen, every physician should

monitor his or her results and refine the approach as needed.

In general, I see patients for clinical follow-up within 1 month, at 6 and 12 months postprocedure, and at least yearly thereafter. At clinic visits, it is routine to query the patients regarding signs and symptoms of DVT, pulmonary embolism, and PTS (eg, lower extremity swelling, heaviness, pain) and examine the lower extremities, abdominal body wall, pelvis, buttocks, and perineal regions. At most visits, a limited ultrasound examination of the proximal veins is performed, and patients with chronic symptoms are also evaluated for saphenous reflux.

ANTITHROMBOTIC DRUG STRATEGIES

In this section, three general scenarios are discussed, for which different degrees of aggressiveness are needed in the prevention of postintervention rethrombosis.

Scenario 1: Straightforward Acute DVT

The first general scenario is the patient who undergoes CDT (any method, including CDT infusion alone, ultrasound-assisted CDT, or pharmacomechanical CDT) for the treatment of acute DVT with a reasonably good technical result and no major factors that should predispose to rethrombosis. Patients in this category should meet these criteria: (1) complete or near-complete thrombolysis was achieved with excellent inflow and outflow (in performing a visual assessment of the quality of flow, a "puff test" should be performed [ie, the physician should briefly puff 3–5 mL of contrast into the vein and observe its transit under fluoroscopy], rather than exerting constant pressure on the syringe, which could artificially create the appearance of flow); (2) any stent placement was limited to the inferior vena cava (IVC) and/or iliac vein; and (3) there are no *major* ongoing clotting risk factors (see the following section for specifics).

In such patients, therapeutic anticoagulation should be resumed immediately postprocedure after hemostasis is achieved using either unfractionated heparin or low-molecular-weight heparin (LMWH). Patients with a lower extremity access site should keep the treated leg immobile for at least 4 hours. After that, early ambulation is highly desirable. Warfarin may be started on the same day as sheath removal, aimed at a target international normalized ratio (INR) of 2 to 3. In warfarin recipients, unfractionated heparin or LMWH should be continued until their INR exceeds 2 for at least 24 hours. The endovascular physician should ideally take responsibility for INR management during the early weeks after treatment to ensure that the patient does not become subtherapeutic due to transitions of care. Anticoagulation should be continued for at least 3 to 6 months, with the ultimate duration reflecting the patient's original DVT risk factors (longer for unprovoked DVT), any ongoing risk factors for recurrent thrombosis, and the patient's individualized risk of bleeding.[9] Although there are no comparative data to support this practice, I routinely use antiplatelet therapy for patients who receive stents. Patients can be seen for follow-up 3 to 5 weeks postprocedure.

If an IVC filter was placed for CDT, it is important for the endovascular physician to ensure that timely filter removal occurs (if appropriate) to minimize the risk of long-term complications such as filter thrombosis, migration, or perforation. Anticoagulation does not need to be stopped for transjugular filter retrieval (unless it is supratherapeutic).

Scenario 2: High-Risk Acute DVT

All patients who undergo CDT should be carefully assessed for major risk factors that may predispose them to rethrombosis. In this context, there are two main groups of major risk factors that may put the patient at higher risk for rethrombosis. The first group is anatomic factors. This includes patients in whom there is significant residual thrombus, poor flow on visual assessment, known compromised popliteal or profunda femoral venous inflow, an inability to re-establish in-line venous outflow (eg, patients with chronic long-segment IVC occlusions that cannot be crossed), or those with stents that are extended caudally into the femoral or (in some cases) common femoral vein. The other group includes biological factors. These are patients with deficiencies of protein C, protein S, or antithrombin III; antiphospholipid antibody syndrome; homozygosity for factor V Leiden or prothrombin gene mutation; combined heterozygosity for both factor V Lieden and prothrombin gene mutations; heparin-induced thrombocytopenia; or active cancer. Of note, I do not consider heterozygosity for the factor V Lieden or prothrombin mutations to confer an increased risk of rethrombosis to a large degree.

In these higher-risk patients, the vascular sheath can be removed while the patient is fully anticoagulated. Because the venous system is a low-pressure system and the venous access site is readily compressible, it is not desirable to allow even a brief subtherapeutic period soon after the procedure. In addition, extended outpatient treatment with LMWH is likely to be a more effective approach to anticoagulation for such patients because it more reliably maintains a therapeutic anticoagulant level and also has anti-inflammatory properties relative to warfarin therapy. Patients with active cancer

should ideally receive LMWH monotherapy as their long-term regimen.[9] Other patients in the higher-risk group may benefit from 1 to 3 months of LMWH followed by a delayed transition to warfarin therapy. In such patients, if stents were placed, then antiplatelet therapy should be used, with strong consideration given to clopidogrel or other thienopyridine antiplatelet drugs if there are no major concerns about bleeding. In such patients, early (1–3 weeks postprocedure) follow-up is desirable to ensure that symptom improvement is occurring as would be expected for the anatomic result achieved, as well as to enable early reintervention should there be suspicion of rethrombosis or another untreated anatomical issue.

In 2012, rivaroxaban received FDA approval for the treatment of VTE, and its use has been increasing exponentially during recent months. Advantages of its use are the once-daily oral dosing, rapid onset of action after administration, the lack of need for blood monitoring or dietary modifications, and the paucity of drug-drug interactions. Clinical studies suggest that rivaroxaban is at least as safe, and possibly safer, as heparin plus warfarin.[10] The main disadvantages of rivaroxaban are the inability to use it in patients with severe renal dysfunction, the rapid loss of anticoagulant effect with missed doses, and the lack of an antidote for use should bleeding occur. Although my experience with rivaroxaban is just beginning, I suggest that it not be used within 6 hours after thrombolysis for now, because there is little data or experience to understand its interactions with thrombolytic drugs. Because many endovascular physicians may not yet be experienced with the use of rivaroxaban, the engagement of a medical thrombosis expert to assist with transitions to and from the different anticoagulants is recommended.

Scenario 3: Established PTS

Endovascular physicians are increasingly called upon to provide salvage treatment options for patients with established, moderate-to-severe PTS. Based on a number of nonrandomized studies supplemented by robust clinical experience, endovascular stent-based recanalization of the obstructed iliac vein can be immensely useful in reducing symptoms, alleviating disability, and improving leg function.[11,12] The available studies suggest that skilled, determined operators can achieve anatomic technical success in more than 80% to 90% of such cases. However, maintenance of stent patency is a significant challenge, with perhaps 40% of stented PTS patients needing additional interventions to address stent patency within 4 to 5 years.[11] As recurrent DVT is frequently present in patients with PTS, this particular population represents a subgroup of DVT patients that is at an exceedingly high inherent risk of rethrombosis.

For this reason, I have adopted a proactive, fairly aggressive posture toward antithrombotic therapy in patients who have been stented. First, before the procedure, I do not stop their anticoagulation unless it is clearly supratherapeutic (eg, INR > 3.5). Second, during the procedure, I liberally use additional boluses of unfractionated heparin to ensure that the patient stays at the higher end of the therapeutic range. Third, I continue LMWH for at least 1 to 3 months postprocedure and encourage patients to delay transition to warfarin for as long as possible. Fourth, I have evolved toward routinely using clopidogrel for long-term therapy unless there is a significant concern for bleeding. The downside of this approach is that some patients will complain of increased bruising with the enoxaparin sodium injections or increased menstrual bleeding—in these situations, I will sometimes replace the clopidogrel with aspirin. I see the patient 1 to 3 weeks postprocedure and maintain a very low clinical threshold for performing surveillance venography with intravascular ultrasound should symptoms continue or return.

COMPRESSION THERAPY

Two European, open-label, single-center randomized controlled trials have found knee-high, 30- to 40-mm Hg, graduated elastic compression stockings (ECS) to reduce the risk of PTS by about 50% when used daily for 2 years after the diagnosis of proximal DVT.[3,13] Based on these studies, clinical practice guidelines advocate routine use of ECS as a key PTS prevention measure.[9]

In December 2012, the results of the SOX trial were presented at the American Society of Hematology Meeting.[14,15] SOX was a multicenter, placebo-controlled, double-blind, North American randomized controlled trial evaluating 806 patients with proximal DVT. All patients received anticoagulation therapy for proximal DVT. Half were randomized to receive 30- to 40-mm Hg, knee-high graduated ECS, and the other half received a placebo stocking. In this study, ECS were found to have provided no clinical benefit—the proportions of patients with PTS at 2 years (assessed using two different validated PTS measures), PTS severity, recurrent VTE, and quality of life were the same in the two treatment arms.

For this reason, after CDT for DVT, I presently suggest to our patients that they can wear ECS to try to reduce symptoms. I inform patients that there are conflicting studies on the point of whether there is any long-term benefit associated with ECS use and encourage their continued use if the patient feels that they are useful in enabling daily activities.

CONCLUSION

Endovascular thrombolytic therapy offers great promise to improve patient outcomes in patients with proximal DVT. Careful attention to diligent clinical follow-up in the immediate postprocedure period, with particular attention to maintaining a therapeutic level of anticoagulation, is essential to optimizing clinical benefit. ■

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