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Postprocedural Management of Patients Undergoing Endovascular Therapy for Acute and Chronic Lower-Extremity Deep Venous Disease

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Endovascular therapy for acute and chronic lower-extremity deep venous disease seeks to improve patency and flow to ameliorate severe symptoms, prevent the postthrombotic syndrome, and treat existing chronic venous disease. Close postprocedure monitoring in the weeks to months following the intervention with implementation of an anticoagulation and symptom management strategy maximizes the likelihood of a durable result. This article outlines several such strategies based on the presenting pathology, results of the intervention, and biological characteristics of the patient.
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Introduction

As the endovascular treatment for lower-extremity deep venous disease has evolved over the past decade and a half, so too has postprocedural care to optimize outcomes. Much of this progress is attributable to improved understanding of deep venous pathophysiology and the medical management of deep venous disease. In spite of this progress, many questions remain to be answered, and there is a relative paucity of data to support one strategy over another. Thus, postprocedure treatment algorithms have been mostly extrapolated from data generated from noninterventional studies and, in some cases, arterial studies.

Endovascular procedures, as outlined in selected articles in this issue, treat superficial venous disease, acute deep venous disease, and chronic deep venous disease. Therefore, the patient population with venous disease is quite heterogeneous; this article focuses on the postendovascular management of the latter 2 pathologies.

In acute thrombotic disease, the goals of postprocedure care are to prevent recurrent thrombosis and optimize flow and patency, both major tenets of the "open-vein" hypothesis.[1] There is considerable evidence that residual obstruction and recurrent thrombosis are significant risk factors for developing the postthrombotic syndrome (PTS). Several studies have demonstrated that the amount of residual thrombus after an acute deep vein thrombosis (DVT), regardless of whether its treated using adjunctive catheter-directed therapy or anticoagulation alone, correlates with the development of PTS.[2-5] Residual thrombus is a risk factor for new thrombus formation, given a baseline flow limitation and potential nidus created by any residual thrombus. Thus, anticoagulation in these patients is essential to maintaining patency. Although elastic compression stockings (ECS) are still a mainstay of therapy for the prevention of PTS, recent data, discussed later in the article, are challenging this practice.

In patients with pre-existing chronic venous disease, optimal symptom management should continue. Regardless of whether chronic venous disease is thrombotic, the postprocedural goals are to prevent new or recurrent thrombosis and relieve existing symptoms. Because studies consistently demonstrate lower primary, primary-assisted, and secondary stent patency rates in patients with thrombosis, a more aggressive postprocedure anticoagulation regimen is indicated for these individuals.[6-9]

Postprocedure Care for Acute Thrombotic Lower-Extremity Deep Venous Disease

Antithrombotic Drugs

As discussed in earlier articles, endovascular thrombus removal can take the form of catheter-directed therapy,

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percutaneous mechanical thrombectomy, or a combination of the both—pharmacomechanical catheter-directed therapy. As part of these maneuvers to remove thrombus, wires, catheters, balloons, stents, and mechanical devices cause significant disruption to the venous endothelium, creating a hypercoagulable state, necessitating intraprocedure anticoagulation. It is essential to continue this anticoagulation into the postprocedure setting, whether it is through unfractionated heparin or low-molecular-weight heparin, to avoid early rethrombosis in a highly thrombotic postprocedure milieu. The interventionalist frequently has to oversee the anticoagulation transition and should have a reasonable understanding of several anticoagulation regimens, the most common of which are outlined here.

Standard Therapy With Transition to Vitamin K Antagonists

Warfarin can be started on the same evening as the procedure, with a goal of titrating the international normalized ratio between 2 and 3. A heparin or low-molecular-weight heparin bridge to warfarin should continue until 2 consecutive international normalized ratios, at most 3 days apart, are in the therapeutic range. This regimen is most appropriate for straightforward acute lower-extremity lysis cases, in which (1) more than 90% thrombus reduction is achieved with restoration of antegrade blood flow and (2) patient factors do not indicate a high risk of rethrombosis. The duration of anticoagulation is discussed later in this section.

Extended Therapy With Low-Molecular-Weight Heparin (LMWH)

As an alternative to the aforementioned therapy, patients may continue using low-molecular-weight heparin for 1-3 months and delay a warfarin bridge. Patients who are at high risk for early recurrent thrombosis could be considered for this regimen. Owing to the labile nature of warfarin therapy, especially during initiation, and the deleterious effects of subtherapeutic anticoagulation,[10] LMWH may provide more consistent anticoagulation. Moreover, LMWH may be more effective at preventing PTS and improving venous patency.[11] Patients can be defined as high risk in several ways. If flow and patency are not adequately achieved during the procedure, perhaps because of an untreatable proximal obstruction or poor inflow from the popliteal vein or a high residual thrombus burden, the patient is more likely to rethrombose and develop worsening symptoms if anticoagulation is subtherapeutic. If a patient has a significant thrombophilia, including protein C or S deficiency, antithrombin III deficiency, a homozygous mutation of factor V Leiden or prothrombin, or antiphospholipid antibody syndrome, extended LMWH therapy is reasonable. Patients with active cancer are recommended to be on LMWH as the primary long-term anticoagulant based on the results of the Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy (CLOT) trial.[12]

Alternative Regimens With the Newer Anticoagulants

In the last several years, a number of new oral agents have emerged to overcome the difficulties associated with warfarin, including its narrow therapeutic window and the large variability in pharmacodynamics necessitating blood monitoring. The most promising are discussed here.

(1) Dabigatran
Dabigatran is an oral agent that works as a direct inhibitor of thrombin (factor IIa). Several trials have demonstrated its utility in venous thromboembolism (VTE). For example, the RE-COVER trial showed similar efficacy and safety to warfarin in the prevention of recurrent VTE or VTE-related mortality in patients with acute pulmonary embolism or proximal DVT.[13] It should be noted that dabigatran is not approved by the United States Food and Drug Administration for VTE.

(2) Rivaroxaban
Rivaroxaban is an oral factor Xa inhibitor that has been approved by the Food and Drug Administration for VTE therapy. The EINSTEIN trials were the pivotal studies that allowed for this approval. The EINSTEIN-DVT trial, a noninferiority randomized trial in patients with DVT without pulmonary embolism, showed a similar rate of recurrent VTE in rivaroxaban-treated patients to that seen in conventionally (LMWH and warfarin) treated patients, with similar bleeding rates.[14] Administration of rivaroxaban is as follows: 15 mg twice daily for 3 weeks followed by 20 mg daily for the rest of the anticoagulation period.

(3) Apixaban
Apixaban is another oral factor Xa inhibitor, it has not been approved for VTE therapy by the Food and Drug Administration. The AMPLIFY trial demonstrated noninferiority of apixaban to conventional therapy in preventing recurrent VTE or VTE-related deaths, with similar bleeding rates.[15]

It should be noted that little data are available regarding the efficacy and safety of these agents following an endovascular procedure, and that extending the results of the noninterventional trials mentioned earlier to post-intervention patients should be done with caution. Moreover, it is unclear how effective these agents are in preventing in-stent thrombosis (if stents were deployed). Although the convenience of these agents is attractive, longitudinal experience is lacking compared with warfarin, and at this time, there are no antidotes to reverse a major hemorrhage. More clinical data need to be gathered before definitive recommendations can be made.

Antiplatelet Therapy

Traditionally, venous thrombotic disease has not assigned platelets a significant role. Current recommendations do not include antiplatelet agents in the initial treatment of a documented episode of VTE. (Aspirin may have a role in extended recurrent VTE prevention, as discussed later.) Nevertheless, after deploying a venous stent, many