Preface
Management of Venous Thromboembolism: Present and Future

An estimated 2 million people in the United States develop venous thromboembolism (VTE) annually. Anticoagulant therapy is the mainstay of VTE treatment. Once the diagnosis of VTE is established, prompt anticoagulation is necessary to prevent thrombus growth and to reduce the risk of pulmonary embolism (PE). At present, rapid anticoagulation can only be effected with parenteral agents. Low-molecular-weight heparin (LMWH) is rapidly replacing unfractionated heparin as the drug of choice for the initial treatment of most VTE patients. Because it can be given subcutaneously once or twice daily without coagulation monitoring, LMWH allows out-of-hospital management of patients with uncomplicated VTE, an approach that reduces healthcare costs and improves patient satisfaction.

Extended anticoagulant treatment is necessary to prevent recurrent VTE. Vitamin K antagonists are the agents most often used for this purpose, and warfarin is the current drug of choice in North America. Recent clinical trials have provided important information regarding the optimal duration and intensity of anticoagulation treatment for patients with VTE. Anticoagulation therapy must be continued until the benefits of such treatment no longer outweigh the bleeding risk associated with long-term anticoagulation. What we have learned in recent years is that the risk of recurrent VTE after stopping anticoagulant therapy is low in patients whose VTE occurred in the setting of well-recognized reversible risk factors, such as surgery. In contrast, the risk of recurrence is high with ongoing risk factors, such as metastatic cancer.

Surprisingly, the risk of recurrent VTE also is high when anticoagulation therapy is stopped in patients whose thrombosis occurred in the absence of any identifiable risk factors, regardless of whether or not there is an underlying thrombophilic defect. Thus, unprovoked thrombosis represents a chronic disease that is characterized by an ongoing risk of recurrence. Extended anticoagulation therapy with warfarin markedly reduces this risk, but the benefit is offset, at least in part, by the increased risk of bleeding with long-term anticoagulation. The balance between these competing risks in each individual patient dictates the optimal duration of anticoagulation therapy. Although LMWH represents an advance over unfractionated heparin, new anticoagulants have the potential to further enhance VTE treatment. For example, fondaparinux, a synthetic analog of the pentasaccharide sequence in heparin and LMWH that mediates their anticoagulant activity, not only shares all the advantages of LMWH over heparin, but also has the added feature that it does not cause heparin-induced thrombocytopenia. Building on these properties, a modified version of fondaparinux, known as idraparinux, has a longer half-life that permits once-weekly subcutaneous injections. Consequently, idraparinux has the potential to be used in place of unfractionated heparin or LMWH for initial treatment of VTE, or as an alternative to warfarin for extended anticoagulation therapy.

New oral anticoagulants also are on the horizon in the form of orally active agents that target thrombin or factor Xa. Of these, ximelagatran, an oral direct thrombin inhibitor, is in the most advanced stages of development. With a rapid onset of action, ximelagatran has the potential to obviate the need for a parenteral anticoagulant for initial VTE treatment. For extended treatment, ximelagatran has potential advantages over warfarin because ximelagatran can be given in fixed doses without routine coagulation monitoring.

In addition to anticoagulants, there are other pharmacological and nonpharmacological treatments for VTE. Another pharmacological option is thrombolytic therapy, a treatment indicated for a subset of VTE patients. Nonpharmacological options for VTE treatment include thrombectomy for acute PE, or for management of chronic thromboembolic pulmonary hypertension. In addition, thrombectomy, with or without concomitant catheter-directed thrombolytic therapy, is used for treatment of selected patients with extensive proximal deep vein thrombosis. Intracaval filters represent another nonpharmacological treatment modality.

This monograph provides a state-of-the-art overview of the management of VTE. Focusing on currently available treatment options, Drs McRae and Ginsberg discuss initial management of VTE, whereas Dr Kearon describes long-term therapy. Using up-to-date information, the authors provide a guide to optimal treatment that can be tailored to the needs of the individual patient. My chapter reviews data on new anticoagulants for VTE treatment, concentrating on those agents that have successfully completed phase 2 or 3 clinical testing. These exciting new drugs have the potential to further streamline VTE treatment. Finally, rounding out the therapeutic options, Drs Augustinos and Ouriel describe nonanticoagulant treatments for VTE, focusing mainly on surgical and percutaneous interventions.

This monograph reviews the strengths and weaknesses of the various treatment options available for VTE. Whether you practice in a hospital or a clinic, frequently or infrequently treat VTE patients, provide short- or long-term care, we trust that this monograph will serve as a useful resource.

Jeffrey I. Weitz, MD
Professor of Medicine and Biochemistry
McMaster University
Director, Henderson Research Centre
HSFO/J.F. Mustard Chair in Cardiovascular Research
Canada Research Chair (Tier 1) in Thrombosis

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