Treatment and Long-Term Management of Venous Thromboembolism

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KEYWORDS

- Venous thromboembolism • Bridge therapy • Switch therapy
- Outpatient venous thromboembolism treatment • New oral anticoagulants

KEY POINTS

- An increased emphasis on risk stratification and standardization may provide a rationale for inpatient versus outpatient treatment of PE and DVT.
- Three options are available when treating patients with new onset VTE: monotherapy, bridging therapy, and switch therapy.
- For provoked VTE, anticoagulation treatment for 3 months is usually considered to be sufficient.
- For unprovoked VTE, treatment for 3 to 6 months should be considered. After that time, patients should be evaluated for the need for extended anticoagulation treatment.
- Newer oral anticoagulants have been developed to overcome the drawbacks of other anticoagulation agents, improve patient care, and simplify and improve VTE management.
- Evidence from several phase III trials suggests that NOACs are effective for secondary prevention of VTE in patients who have completed standard anticoagulation therapy.

INTRODUCTION

The term "venous thromboembolism" (VTE) covers a range of conditions from deep vein thrombosis (DVT) to pulmonary embolism (PE), all of which can be life-threatening. Thrombi that form in lower-extremity veins can embolize, leading to occlusion of the pulmonary vasculature. As a reflection of this pathophysiologic relationship, most patients with symptomatic PE have DVT and many patients with DVT

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have asymptomatic PE.[1] The aims of treatment are to alleviate symptoms, to minimize acute morbidity and mortality by preventing the extension or potentially fatal embolization of the initial thrombus, and to avoid postthrombotic syndrome. The anticoagulants heparin and dicumarol were discovered serendipitously in 1916 and 1939, respectively, and heparin has been commercially available to treat blood clots since 1940. In the 1970s, three different research groups in Stockholm, London, and Ontario began work on low-molecular-weight heparin (LMWH) and by the mid-1980s, LMWH preparations were being tested in clinical trials. LMWH first became commercially available in 1993, and was followed by the introduction of fondaparinux and bivalirudin. Because of the advantages of LMWHs compared with unfractionated heparin (UFH) (**Box 1**), LMWHs have now replaced heparin for most indications. However, their parenteral administration and their restricted use in patients with renal failure limit their use. In the 2010s, a new era of oral anticoagulation has started (**Fig. 1**).

PHASES OF ANTICOAGULATION

Anticoagulant therapy, the mainstay of treatment of VTE, has two goals. First, anticoagulant therapy treats or "turns off" the acute episode of thrombosis, which improves acute symptoms, prevents thrombus extension, and reduces the risk of early PE. Second, anticoagulant therapy prevents new episodes of VTE that do not arise directly from the acute episode of thrombosis.[2] There are two main phases during anticoagulation therapy: the acute (ie, active treatment) and chronic phases (ie, secondary prevention) (**Fig. 2**).

Acute Phase

In the acute phase, the risk of thrombus extension and PE is high, but the initiation of treatment rapidly reduces this risk.[3,4] Therefore, it is critical that anticoagulant therapy is started as soon as possible when VTE is diagnosed (or is highly suspected).[3] Moreover, because there is a high risk of VTE progression in the acute phase, the use of a higher-intensity anticoagulant therapy at the start of treatment is recommended.[2,5–7] Furthermore, if anticoagulant therapy is stopped before treatment of the acute episode of thrombosis has been completed, there may be reactivation of the initial thrombosis with a further increase in the risk of recurrent VTE.[2,5–7] Four observations support duration for anticoagulant therapy for approximately 3 months for active (acute) treatment of VTE.[2,5–7] These reports suggest that treatment for 3 months is associated with the same risk of recurrent VTE as treatment for 6 months or longer, suggesting that 3 months is adequate therapy.[2]

Box 1
Advantages of LMWH compared with UFH

- Less binding to plasma proteins so more predictable dosing response
- Lower incidence of HIT
- Less or no monitoring needed
- Less osteopenia
- Does not cross the placental barrier
- Fixed, weight-based dose

Abbreviations: HIT, heparin-induced thrombocytopenia; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.