Contemporary Treatment of Venous Thromboembolic Disease

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KEYWORDS

• Venous thromboembolism • Deep vein thrombosis • Pulmonary embolism • Anticoagulation • Thrombolysis • Inferior vena cava filter

KEY POINTS

- The routine use of thrombolysis for lower-extremity deep vein thrombosis (DVT) is not recommended.
- Catheter-directed thrombolysis is suggested in patients with impending venous gangrene whose symptom duration is less than 14 days and who have a low risk of bleeding.
- Systemic thrombolysis, administered through a peripheral intravenous line, is recommended in patients with hemodynamic collapse (ie, persistent hypotension).
- The new target-specific oral anticoagulants have been shown to be as safe and effective as standard anticoagulation for the treatment of acute venous thromboembolism (VTE).
- Indefinite anticoagulation is suggested in patients with an unprovoked or recurrent VTE and in patients with an active malignancy.

INTRODUCTION

Venous thromboembolism (VTE) encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE). The incidence of VTE is approximately 1 per 1000 person-years.[1,2] The case-fatality rate in patients presenting with an acute DVT and PE during the first 3 months of anticoagulation is 9.0% and 30.1%, respectively.[3] In addition to mortality, the cumulative incidence of chronic thromboembolic pulmonary hypertension is approximately 4% at 2 years following a diagnosis of PE.[4] Furthermore, postthrombotic syndrome (PTS) occurs in 20% to 50% of patients diagnosed with a symptomatic DVT.[5] The treatment of VTE is divided into 3 phases (**Fig. 1**).[6] Several target-specific oral anticoagulants (TSOACs) have been studied for the treatment of VTE during these phases of therapy (**Tables 1** and **2**) and have been shown to be as noninferior in safety and efficacy as conventional therapy. This article reviews the contemporary treatment of VTE.

RISK STRATIFICATION (INPATIENT VS OUTPATIENT TREATMENT)

A *Cochrane Review* of randomized controlled trials (RCTs) demonstrated the efficacy and safety of the outpatient treatment of DVT with low-molecular-weight heparin (LMWH) compared with inpatient anticoagulation.[7] Several clinical prediction rules have been established to stratify PE-related mortality risk,[8–10] of which the Pulmonary Embolism Severity Index seems to be the best validated

The authors have nothing to disclose.
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Cardiol Clin 33 (2015) 49–57
http://dx.doi.org/10.1016/j.ccl.2014.09.007
0733-8651/15/$ – see front matter

(Table 3).[6] The use of LMWH as outpatient treatment of patients with low-risk PE has been shown to be safe and effective in several RCTs and a systematic review.[11–13]

THROMBOLYSIS FOR LOWER EXTREMITY DEEP VEIN THROMBOSIS

There are no RCTs comparing catheter-directed thrombolysis (CDT) with systemic thrombolysis for lower-extremity DVT. Lower-quality evidence suggests that CDT is more effective in establishing vein patency and is associated with a lower risk of bleeding compared with systemic thrombolysis.[6] A meta-analysis of thrombolysis (either systemic or catheter-directed) for lower-extremity DVT demonstrated a significant difference in clot lysis, vein patency, and reduction of PTS in patients treated with lytic therapy compared with standard anticoagulation at the expense of more bleeding complications.[14] There are insufficient data to recommend one thrombolytic agent over others. CDT is suggested in patients with an ileofemoral DVT with the following criteria: impending venous gangrene, symptom duration less than 14 days, good functional capacity, life expectancy greater than 1 year, and low risk of bleeding. In the absence of impending limb gangrene, standard anticoagulation is an acceptable, initial form of treatment.[6] The use of venous stents following balloon angioplasty in patients with residual occlusion after CDT has not been studied in prospective, randomized trials.

THROMBOLYSIS FOR PULMONARY EMBOLISM

Features of right ventricular dysfunction as determined by echocardiography, CT scanning, or an elevation of cardiac biomarkers (ie, troponins, brain natriuretic peptide) are associated with worse outcomes in patients with an acute PE.[15] However, systemic thrombolysis was not associated with a reduction in mortality in patients with a submassive PE (abnormal right ventricular dysfunction without arterial hypotension) in 2 randomized, double-blind studies.[16,17] In the most recent RCT using thrombolysis in patients with a submassive PE, major bleeding and hemorrhagic stroke occurred in approximately 12% and 2%, respectively, in patients treated with thrombolysis (statistically significant).[17] Systemic thrombolysis is recommended in patients who experience hemodynamic compromise.[6] There is insufficient evidence to recommend the administration of

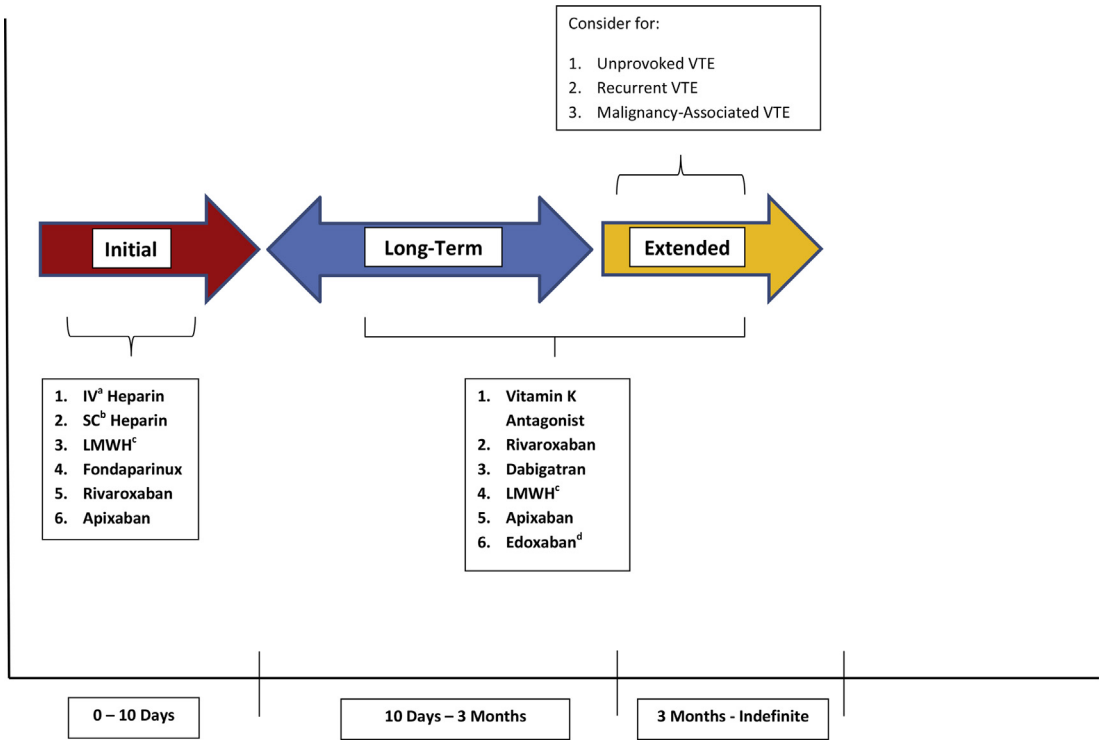

Fig. 1. Phases of anticoagulant treatment. (a) Intravenous; (b) subcutaneous; (c) LMWH, preferred in patients with a malignancy; (d) edoxaban has not yet been approved for VTE treatment.