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# The Management of Venous Thromboembolic Disease

## New Trends in Anticoagulant Therapy

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• Deep vein thrombosis • Anticoagulation • Extended treatment • Iliofemoral DVT • Femoropopliteal DVT • Distal (calf) DVT

**Key points**

- Based on ease of dosing and large noninferiority trials, direct oral anticoagulants (DOACs) should be considered first-line therapy for treatment of venous thromboembolism (VTE).
- New strategies for treatment (besides long-term anticoagulation) of unprovoked (idiopathic) VTE now exist: prophylactic dose rivaroxaban or apixaban, aspirin, and use of HERDOO2 scoring rule to identify women at low risk of VTE recurrence.
- Aggressive pharmacomechanical thrombolysis appears indicated for iliofemoral deep vein thrombosis (DVT) to decrease immediate symptoms.
- Controversy still exists on the role of anticoagulation after calf vein thrombosis.

## INTRODUCTION

In the past several years, the Food and Drug Administration (FDA) has approved 5 new direct oral anticoagulant (DOAC) agents. In the 2012 American College of Chest Physicians (ACCP) recommendations, vitamin K antagonists (VKAs) remained the central mainstay of therapy for treatment of acute VTE [1]. In the 2016 ACCP guidelines, DOACs gained preference over VKAs

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as first-line therapy for the treatment of venous thromboembolism (VTE). With these new agents, an explosion of clinical studies is occurring to determine the utility of each medication for several different indications. This article discusses how to choose the best anticoagulant for VTE treatment and when extended anticoagulation for prevention of recurrent VTE should be used, and specific discussions are provided on calf vein DVT and iliofemoral DVT.

## SIGNIFICANCE

### Anticoagulant choice for venous thromboembolism

Approved in 1954, VKAs (warfarin [Coumadin]) have been the mainstay of therapy for thrombotic diseases for greater than a half century. Given the established safety profile of VKAs and their efficacy in reducing the risk for recurrent thrombosis and fatal pulmonary embolism (PE), they represent the gold standard against which every new agent is compared. There are several shortcomings associated with VKAs, not the least of which is that they have a defined bleeding risk of 5% to 6% per year [2], which cannot be mitigated by targeting a lower International Normalized Ratio (INR) [3,4]. Other shortcomings include that they require monitoring and that the metabolism of the drug is affected by diet and many commonly prescribed medications. Until recently, few alternatives existed other than low-molecular-weight heparins (LMWHs). Despite the downside of subcutaneous administration with the need for daily or twice-daily home injections, the LMWHs hold several advantages: predictable weight-based dosing, routine laboratory monitoring not necessary in most circumstances, and efficacy similar to VKAs. In a pooled analysis of the treatment of VTE involving LMWH and VKAs, the rate of fatal PE during treatment of DVT was 0.4% and of all PE was 1.5%, with the rates similarly low after cessation of anticoagulation [5]. In several circumstances, LMWHs are superior to VKAs. For example, in patients with malignancy, treatment with LMWH decreased the risk of recurrent VTE by approximately 50% at 6 months to 1 year compared with warfarin without an increase in bleeding [6]. In the Home-LITE (Home therapy of venous thrombosis with long-term LMWH versus usual care: patient satisfaction and post-thrombotic syndrome) trial, tinazparin (a LMWH), was superior to warfarin for prevention of post-thrombotic syndrome (PTS), development of leg ulcers, and treatment satisfaction after significant DVT [7].

Although VKAs and LMWH remain important agents for the treatment of VTE, there has been rapid development of evidence supporting the use of DOACs. The 2 categories of DOACs are the direct thrombin inhibitors and factor Xa inhibitors. Currently, of the direct Xa inhibitors, apixaban, rivaroxaban, and edoxaban have all been FDA approved for the treatment of VTE, whereas dabigatran is the approved direct thrombin inhibitor. The DOACs are appealing because they are all administered orally, do not need monitoring, and have fixed doses that do not need to be weight based adjusted. Two major initial clinical concerns regarding these agents is their efficacy/safety and reversibility in the event of major bleeding. In the past 10 years, all the DOACs each have had at least 1 large randomized controlled trial demonstrating noninferiority in the