Treating Acute Venous Thromboembolism — Shift with Care
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Venous thromboembolism is the third leading cause of vascular death, with a high incidence, especially among older persons. Incidence rates increase from 1 per 10,000 annually among persons less than 40 years of age to nearly 1% annually among persons 80 years of age or older; more than one third of cases occur in persons older than 60 years of age. The mainstay of treatment for more than a generation of physician experience involves bridging anticoagulation therapy from a parenteral heparin-type anticoagulant to a vitamin K antagonist such as warfarin, which requires laboratory monitoring. Given the rapid expansion of knowledge about venous thromboembolism and its treatment, it is important to carefully consider how to translate knowledge regarding new treatments into clinical practice.

Now in the Journal, Agnelli et al. report on the next in a line of trials testing the use of unmonitored, new oral anticoagulants in the treatment of acute venous thromboembolism. The investigators randomly assigned 5400 patients with acute deep-vein thrombosis or pulmonary embolism in double-blind fashion to receive apixaban, at a dose of 10 mg twice daily for 7 days followed by 5 mg twice daily for 6 months, or conventional therapy with subcutaneous enoxaparin bridging to warfarin for 6 months. Apixaban was noninferior to conventional therapy for the primary end point of symptomatic recurrent venous thromboembolism or death related to venous thromboembolism, which occurred in 2.3% of patients who received apixaban and in 2.7% who received warfarin. The risk of major bleeding favored apixaban; major bleeding occurred in 0.6% of patients, as compared with 1.8% of patients who received warfarin. Including this study as well as trials of rivaroxaban and dabigatran, the reported experience comparing new oral anticoagulants to conventional treatment now includes more than 15,000 patients. Notably, the current trial had many exclusion criteria, and the study was completed in 28 countries, with no results provided according to geographic region. For these and other reasons, much additional information is needed.

How can practitioners translate the knowledge from this and other, similar trials into practice? Currently, in the United States, rivaroxaban is the only new oral anticoagulant approved by the Food and Drug Administration for the treatment of acute venous thromboembolism; dabigatran is being used off-label. To optimize the use of new anticoagulants in the treatment of patients with acute venous thromboembolism at our center, my colleagues and I created a protocol incorporating six key factors to ensure high-quality care (Table 1).

New anticoagulants are not for every patient, and there is ongoing research to optimize the use of vitamin K antagonists, so it is unlikely that these will disappear from practice. Advances during the past decade include the emergence of prothrombin-time self-testing, anticoagulation clinics, the diminished frequency of monitoring for selected patients, and the potential for basing dosing decisions on genetic information. As we translate knowledge from the era of vitamin K antagonists to new agents, it is critical that we consider the factors discussed here. More information is needed on reversal strategies, monitoring (e.g., in the presence of interacting drugs, extremes of patient weight, or bleeding or thrombosis complications), approaches to treatment failure, comparisons of adherence to treatment among new drugs and warfarin, and formal cost-
A New Era in the Treatment of Amyloidosis?

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Amyloidosis is a diverse group of diseases caused by extracellular accumulation of protein in a highly ordered, abnormal, insoluble fibrillar form. These diseases can be hereditary or acquired and localized or systemic. Most are progressive and fatal. Among the almost 30 different proteins that have been found to form amyloid in humans, transthyretin, a carrier molecule of