Issues in the Management of VTE

Written by Mary Beth Nierengarten

What are the long-term consequences for a patient after a blood clot, and how does this inform management of venous thromboembolism (VTE)? These issues were addressed in a session at the 2014 American Thoracic Society conference during which a panel of experts discussed a number of topics, including the use and efficacy of novel anticoagulants, thrombolytics for pulmonary embolism (PE), and the development of chronic thromboembolic pulmonary hypertension (CTEPH).

NOVEL ANTICOAGULANTS

Victor F. Tapson, MD, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California, USA, spoke regarding novel anticoagulants for VTE, emphasizing the equivalent safety and efficacy profile compared to warfarin, marking a new era of prevention and treatment of VTE.

Dr. Tapson presented data on the 4 novel oral anticoagulants—namely, apixaban, edoxaban, rivaroxaban, and dabigatran—but focused on the latter 2, which have been approved by the US Food and Drug Administration for use in VTE (Table 1).

Table 1. Food and Drug Administration–Approved New Coagulants

Key Studies	Key Points
	Rivaroxaban
The Einstein Group *N Engl J Med* 2010. The Einstein Group *N Engl J Med* 2012.	Indicated for initial treatment of DVT and PE Indicated for reduction of recurrence risk of PE and DVT after initial 6 months of treatment Avoid use in patients with CrCl<30 mL/minute No adequate trials in pregnant women
	Dabigatran
Schulman S, et al. *N Eng J Med* 2009. Schulman S, et al. *N Eng J Med* 2013.	Approved for the treatment of PE and DVT in patients treated with parenteral anticoagulant for 5 to 10 days Avoid concomitant use of P-glycoprotein inhibitors or in patients with CrCl<50 mL/minute No adequate trials in pregnant women

CrCl=creatinin clearance; DVT=deep vein thrombosis; PE=pulmonary embolism.

Overall, the data from these trials show that compared with warfarin, the novel oral anticoagulants are non-inferior in terms of efficacy, with similar or lower bleeding rates. This translates to simpler therapy, given the lack of need for drug-level monitoring and fewer drug-drug interactions.

The safety and efficacy profile is less well described in specific populations—namely, older patients and those with submassive PE and iliofemoral deep vein thrombosis, cancer, and extremes of weight. In addition, a number of questions remain regarding cost-effectiveness and delivery-related issues—specifically, pretreatment with low-molecular-weight heparin, overdose and reversal, discontinuation and restart for surgery, and concurrent use with antiplatelet agents.

Overall, Dr. Tapson cited the clear advantages of the new anticoagulants but emphasized that all can cause bleeding.

Official Peer-Reviewed Highlights From
ATS 2014
Where today's science meets tomorrow's care™

DURATION OF ANTICOAGULATION FOR VTE OR SECONDARY PROPHYLAXIS

Todd M. Bull, MD, Director of the Pulmonary Vascular Disease Center, University of Colorado, Denver, Colorado, USA, argued that the duration of therapy is more nuanced than what the guidelines suggest and so requires participation from patients to individualize and maximize secondary prevention of VTE.

The nuance stems from data suggesting that the risk of recurrent VTE in patients who have had an initial unprovoked VTE is significantly elevated when they stop anticoagulation and is thus analogous to a chronic disease. Data from a study by Agnelli and colleagues showed a comparable recurrent risk of VTE at 2 years in patients who discontinued anticoagulation after 3 months and those who discontinued anticoagulation at 1 year, despite a substantial initial risk recurrence in the patients who stayed on anticoagulation for 1 year [Agnelli G et al. *N Engl J Med* 2001]. Other studies have shown similar risk profiles. The risk of recurrent clot, however, must, of course, be weighed against the bleeding risk on chronic anticoagulation.

Dr. Bull suggested that, given the chronic risk of recurrent VTE, clinicians should help patients weigh the benefits and risks of anticoagulation. Stratifying patients based on the type of risk can help—that is, provoked (eg, surgery, birth control pills) versus unprovoked (ie, previous idiopathic clot). Data show that patients with provoked risk have approximately a 3% annual risk of recurrent VTE after discontinuing anticoagulation, or about 15% risk at 5 years. If the VTE is unprovoked, data show that there is 10% risk of another clot in the first 2 years after stopping anticoagulation and a 30% risk of recurrence at 5 years. In comparison, the annual risk of major bleeding on vitamin K antagonists is approximately 1% to 4% per year but may be lower with the newer oral Xa inhibitors.

Overall, Dr. Bull emphasized the need for patient education and a careful discussion and understanding of the patient's goals (ie, personal perspective on risks of clot versus bleeding) and for clinicians and patients to work together to balance the risks and benefits of anticoagulation.

DEVELOPMENT OF CTEPH

Timothy A. Morris, MD, Department of Medicine, Division of Pulmonary and Critical Care Medicine, University of California, San Diego Medical Center, San Diego, California, USA, spoke on "connecting the clots," or the process by which people go from acute to chronic thromboembolic disease. Although the development of CTEPH is not common after an acute PE, it does occur, and it needs to be recognized and addressed.

Dr. Morris argued that the term "chronic" is a misnomer; rather, these clots represent "living" tissue that continues to grow with its own blood supply. He theorized that an acute clot transitions to "living" tissue where there is a resistance to lysis, persistence of ligands, abnormal clot structure, and presence of remodeling cells. He closed by proposing a new way of looking at the development of CTEPH, where there is a spectrum of recovery from acute PE, with CTEPH representing partial or absent recovery.

THROMBOLYTICS FOR PE

Stavos V. Konstantinides, MD, Center for Thrombosis and Hemostasis, University of Mainz, Germany, ended the session with a presentation on thrombolytic therapy in PE, emphasizing that the importance of this "old" therapy is not on the thrombolytic drugs themselves but on the risk-adjusted management of acute PE, whether revascularization or reperfusion is needed for patients with intermediate-risk PE; the safety of thrombolysis; and the alternative treatment options. Among the key points that he highlighted from recent clinical trials are the need for early revascularization or reperfusion therapy in patients with imaging-detected acute right ventricular dysfunction and myocardial injury, even if they appear stable at diagnosis; the importance of patient age when selecting candidates for thrombolytic treatment among intermediate-risk patients; and a 50% dose reduction as a potential alternative strategy for patients with a high bleeding risk.