Venous thromboembolism: “...an ounce of prevention is worth a pound of cure”

Samuel Z. Goldhaber¹; Walter Ageno²

¹Harvard Medical School, Thrombosis Research Group, Brigham and Women’s Hospital, Boston, Massachusetts, USA; ²Department of Internal Medicine and Thrombosis and Haemostasis Unit, University Hospital of Varese, Varese, Italy

Pulmonary embolism (PE) and deep-vein thrombosis (DVT), collectively known as venous thromboembolism (VTE), constitute the third most common cause of cardiovascular death, after myocardial infarction and stroke (1). VTE, more than myocardial infarction or stroke, can strike at any age, including those who at first glance appear to be young and healthy (Figure 1). The incidence of myocardial infarction is plummeting. Stroke incidence, which had been increasing, has now plateaued. However, the incidence of PE and DVT is increasing over the past decade (2). The reasons for this phenomenon are multifactorial. Improved diagnostic technology is only part of the explanation. Other explanations include an increasingly elderly population, more surgical procedures with thrombosis-associated complications, and more patients with medical illnesses that have inflammatory components (such as diabetes, metabolic syndrome, and chronic kidney disease) predisposing them to VTE.

As lifelong students of VTE, we jumped at the opportunity to edit a Theme Issue devoted to VTE in *Thrombosis and Haemostasis*. The topic of VTE provides necessary balance and perspective to other Theme Issues that focus on arterial thrombosis. What the reader will find is that there are more similarities than differences between venous and arterial thrombosis. We should therefore be “lumping” rather than splitting. VTE is one of the major components of vascular medicine, along with coronary disease, stroke, and peripheral arterial disease. It has been fun to collaborate on this project and to work together to put an international flavour to this Theme Issue with North American and European perspectives.

We have commissioned state-of-the-art reviews on the following VTE topics: epidemiology, diagnosis, acute treatment with anticoagulation, advanced therapy including thrombolysis, the optimal duration of anticoagulation, and primary prevention. Each review is a scholarly work with up-to-date references, tables, and figures to serve as a jumping off point for further study of a particular VTE subtopic.

To start out, Nicoletta Riva and colleagues (3) teach us in their review of epidemiology and pathophysiology that we should resist the temptation to classify PE and DVT as “unprovoked” when an obvious classical cause is not apparent. They make the important point that with careful scrutiny, we can often detect minor predisposing conditions such as chronic inflammatory disorders, infectious diseases, and traditional cardiovascular risk factors. They emphasise that inflammation could link all risk factors and also serve as the pathophysiological bridge between arterial and venous thrombosis.

Then Marc Righini and colleagues (4) provide us with a roadmap for rational, safe, and cost-effective diagnostic strategies to detect and to exclude PE and DVT. This roadmap is not as straightforward as one might think. Curves, bumps, and roadblocks are encountered when dealing with elderly patients, pregnant women, or patients with a prior VTE. Another vexing problem, which they confront head-on, is how to deal with thorny diagnostic and management issues centering on isolated calf DVT and tiny subsegmental PE.

Christopher Hillis and Mark Crowther (5) next tackle the increasingly complex choices that we clinicians confront when deciding which anticoagulant(s) to select for treating newly diagnosed acute VTE. Our array of choices has increased far beyond the traditionally available unfractionated heparin, low-molecular-weight heparin, fondaparinux, and warfarin. To anticoagulate acute VTE, we now have (in the United States) four licensed non-vitamin K antagonist oral anticoagulants (NOACs) which are also known to the broader population of healthcare providers as “novel oral anticoagulants.” They are, in chronological order of obtaining approval from the Food and Drug Administration for VTE treatment: rivaroxaban, apixaban, dabigatran, and edoxaban. All but edoxaban are also approved for VTE treatment by the European Medicine Agency.

In some patients with intermediate risk (submassive) or high risk (massive) PE, and in some patients with iliofemoral or large femoral DVT, anticoagulation alone is not sufficient therapy. Stavros Konstantinides and his co-author Simone Wärntges (6) delve into when and how to consider employing advanced therapies: systemic fibrinolysis and pharmacomechanical therapy. Catheter-directed, ultrasound assisted, low-dose fibrinolysis for PE has sparked particular interest because low dose tissue plasminogen activator (the FDA approved dose is 24 mg, for example), compared with administration of standard 100 mg through a peripheral vein, is thought to be
associated with a lower risk of catastrophic bleeding such as intracranial haemorrhage. Perhaps the most controversial topic in VTE therapy is the optimal duration of anticoagulation. Paolo Prandoni was one of the first investigators to point out the high rate of recurrent VTE after discontinuation of anticoagulation. He and his colleagues from the University of Padua (7) discuss the array of options available when we confer with our patients about this crucial topic. Do we focus on risk stratification with D-dimer testing and repeat venous ultrasound of the deep leg veins? Or do we focus on choosing a long-term extended strategy, either using a NOAC or low dose aspirin? Read this review to help guide your discussion with the patient, family, and professional colleagues.

One of the most iconic Americans, Benjamin Franklin, quipped that “an ounce of prevention is worth a pound of cure.” This is particularly true for PE and DVT. Serena Granziera and Alexander T. Cohen (8) provide a comprehensive update on VTE primary prevention, with a focus on hospitalised medical patients and orthopaedic surgical patients. They teach that the risk of VTE extends for months after hospitalisation for medical illness and for months after an orthopaedic surgical procedure.

We are grateful to our contributing authors. For them and for us, working on this project was a labour of love. This Theme Issue will be on top of our desks, ready for our quickly looking up the latest teachings from global thought leaders.

Conflicts of interest
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References