

Editorial Focus

Improving clinical outcomes for patients with cancer-associated thrombosis

Ajay Kakkar

Barts and The London School of Medicine and Dentistry and Thrombosis Research Institute, London, UK

Venous thromboembolism is a common complication in patients with malignant disease. Its management is attended by both a high risk for recurrent thromboembolism and for antithrombotic therapy-associated bleeding complications (1). Beyond the problems of recurrent thrombosis and bleeding, therapy for cancer-associated thrombosis also has a substantial impact on quality of life for patients already coping with the rigorous demands of often complicated anticancer therapy. Thus, any antithrombotic intervention for the longer treatment of venous thromboembolism (VTE) in the cancer patient should not only impact on recurrent thromboembolism and reduce the risk of bleeding but also improve quality of life (2).

In recent years, attempts have been made to overcome the limitations of chronic oral anticoagulant therapy with vitamin-K antagonists in this potentially fragile population of patients. Interventions evaluating extended duration of low-molecular-weight heparin therapy to prevent recurrent thromboembolism have established a new standard for antithrombotic therapy in these groups of patients (3). However, a number of issues remain to be resolved. These include the duration of antithrombotic therapy to prevent recurrent thromboembolism in cancer patients after a first thromboembolic episode; the intensity of anticoagulation required in such patient populations over an extended duration; and the ability to predict the risk of anticoagulant-associated bleeding versus benefit in terms of preventing recurrent thromboembolism for an individual patient.

In this issue of *Thrombosis and Haemostasis* Trujillo-Santos et al. publish an interesting paper derived from the RIETE registry describing the three-month clinical outcomes for 3,805 cancer patients with acute VTE (4). Using this large data set they have been able to identify a number of characteristics associated with a higher risk for either recurrent pulmonary embolism (PE), deep-vein thrombosis or major anticoagulant-associated bleeding. The predictive factors associated with a higher risk for recurrent PE and recurrent deep-vein thrombosis included age under 65 years and a diagnosis of malignant disease within the three months prior to initial presentation with VTE. Additionally,

clinically overt PE as first presentation of thrombosis was associated with a higher risk for subsequent recurrent PE. In terms of the major bleeding, factors associated with this complication of anticoagulant therapy included recent major bleeding, renal impairment, immobility and metastatic cancer. Interestingly for major bleeding immobility might have been associated with a poor performance status, and the other predictive factors could have been more frequently seen in those more likely to be considered clinically fragile patients and those with a poorer prognosis.

Although this potential predictive model needs prospective validation as its implications in terms of providing or withholding anticoagulant therapy, particularly over a much extended duration when patients remain at risk for recurrent thromboembolism are wide-ranging. Clearly establishing the balance between benefit and risk for anticoagulation at the outset of therapy for thromboembolic disease in patients with cancer has the potential to greatly improve outcomes in this challenging clinical population. A predictive model based on patient characteristics could provide immediate clinical utility and thus improve the chances of its widespread adoption. However, as the authors identify themselves, factors such as an individual patient's performance status, and type of therapeutic intervention for cancer were not included in this registry. The impact of the type of anticancer therapy should not be underestimated, both at the time of presentation with VTE and as therapy changes during the course of the natural history of the cancer itself.

Equally, the impact of primary tumour site, recently demonstrated to be of predictive value for a primary thromboembolic event (5), does not appear to have the same importance in terms of recurrent VTE, a discrepancy worthy of further evaluation as the findings from the RIETE registry are tested in a prospective cohort. In addition to the evaluation of patient characteristics in predicting these outcomes associated with anticoagulant therapy, the use of biomarkers, in particular those based on the evaluation of circulating tissue factor-bearing microparticles, may add further valuable information (6). The introduction of such bio-

Correspondence to:

Prof. Ajay Kakkar
Centre for Surgical Sciences
Barts and The London Queen Mary School of Medicine
London, United Kingdom
Tel.: +44 207 351 8309, Fax: +44 207 351 8317
E-mail: akk@tri-london.ac.uk

Received August 11, 2008
Accepted August 11, 2008

Prepublished online August 14, 2008
doi:10.1160/TH08-08-517

Thromb Haemost 2008; 100: 367–368

markers will require the same rigorous prospective assessment as the potential clinical models. Nevertheless, the findings of the RIETE registry provide a useful insight into this challenging

clinical problem and give an important opportunity to focus further research effort in helping to improve clinical outcomes for cancer patients.

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