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CLINICAL OBSERVATIONS

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Thromboprophylaxis in cancer outpatients

Carine J. M. Doggen LEIDEN UNIVERSITY MEDICAL CENTER

In this issue of *Blood*, Khorana and colleagues report a simple and practical model for the prediction of symptomatic venous thrombosis after the initiation of chemotherapy in cancer outpatients.

Thromboprophylaxis may prevent the occurrence of venous thrombosis, an important cause of morbidity and mortality among patients with cancer, especially those on active antitumor therapy. Identifying cancer patients at high risk for thrombosis who might benefit from prophylaxis is still a major challenge. The only well-defined high-risk group for which thromboprophylaxis appears to be effective and relatively safe is surgical patients,[1,2] although prophylaxis is also recommended for acutely ill medical patients.[3,4] However, a high-risk group of outpatients with cancer remains to be determined, and is a necessary piece of information to obtain before the appropriateness of thromboprophylaxis can be assessed.

In this issue of *Blood*, Khorana and colleagues develop a simple and practical model for the prediction of symptomatic venous thrombosis after the initiation of chemotherapy, among outpatients with different types of malignancies. Primary site of cancer, platelet count, leukocyte count, hemoglobin level, use of erythropoiesis-stimulating agents, and body mass index were found to be predictive factors.

The authors make excellent use of data available from the Awareness of Neutropenia in Chemotherapy Study Group Registry, an observational multicenter follow-up study.[5] The original goal of this study was to assess febrile neutropenia and related complications. Symptomatic venous thrombotic events were recorded when reported by physicians. Due to this design, the occurrence of asymptomatic thrombotic events could not be assessed. However, the clinical importance of such events is still unknown. The authors used a split sample approach, appropriately developed a risk model based on clinical and laboratory variables, and studied both derivation and validation cohorts.[6,7]

Based on the predictive factors, patients were classified into low-risk (27%), intermediate-risk (61%), and high-risk (12%) groups. Most thrombotic events (75%) occurred during the first 2 cycles of chemotherapy. In the low-risk group, only 0.6% developed symptomatic venous thrombosis, compared with 1.9% in the intermediate-risk group. These findings suggest that the 88% of the patients in the low- and intermediate-risk groups are unlikely to benefit from prophylactic anticoagulation.

Patients in the high-risk group had a nearly 7% risk of developing venous thrombosis during a median follow-up period of 73 days. One may argue whether a 7% risk warrants thromboprophylaxis; 93% of patients in this high-risk group would be treated without any apparent benefit, and moreover, patients with a malignancy have an increased risk of major bleeding during thromboprophylaxis.[8] To make a balanced decision, the risks and benefits need to be assessed. Unfortunately, data regarding bleeding risk were unavailable in the study by Khorana et al. Similarly, data on prophylactic anticoagulation use was lacking. If one of the investigated factors instigated the use of anticoagulation, and thereby indirectly decreased the risk of venous thrombosis, this would influence the model.

This was a very large study consisting of more than 4000 patients with different types of malignancies. Most patients had an excellent performance status. Only a few patients with less prevalent malignancies strongly associated with venous thrombotic events, such as brain tumors, were included. One has to be careful in generalizing the results to patients with a poor performance status and patients with these less prevalent malignancies, as other predictive models may more closely fit those cases.

The authors had the opportunity to use a split sample approach to validate the model. However, further studies are needed to validate this model in other external large follow-up studies of outpatients with malignancies. Additional clinical factors not investigated in the present study, such as previous history of venous thrombosis and anticoagulation use, should be included. As the authors indicate, the risk model may indeed be used in the design of clinical trials involving cancer outpatients that would benefit from thromboprophylaxis.

Conflict-of-interest disclosure: The author declares no competing financial interests. ■

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