Preventing Venous Thromboembolism in Cancer Patients: Can We Do Better?

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On September 15, 2008, a Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism was put forward by the US Surgeon General. The association between cancer and thrombosis has been known for more than 140 years. Approximately one in five episodes of venous

thromboembolism (VTE) occurs in patients with a diagnosis of cancer. In addition to the release of cytokines and procoagulants by tumors resulting in a hypercoagulable state, patients with cancer seem to fulfill the Virchow's Triad, which includes compromised functional status and blood vessel compression or invasion by tumors. The risk of VTE is increased further by treatment, including surgery, chemotherapy, hormonal therapy, and more recently, antiangiogenesis agents. It is estimated that 4% to 20% of cancer patients will develop a symptomatic VTE during the course of their disease. The true frequency of VTE is clearly greater, given that asymptomatic VTE may be found on routine imaging studies or at the time of postmortem examination.^{1,2} Hospitalized patients with cancer are at a particularly high risk for VTE because of the serious nature of their illness, immobilization, and frequent invasive procedures. The reported occurrence of VTE in patients with cancer has increased during the last two decades. This is a result of improved diagnosis as well as the use of more aggressive systemic therapies.³ Patients with cancer who have established VTE are at greater risk of recurrence and early mortality, making VTE a leading cause of death among patients with cancer.⁴⁻⁷

Although hospitalized patients with cancer are at increased risk of VTE, to our knowledge, no randomized controlled trial of VTE prophylaxis that specifically addressed hospitalized patients with cancer has been reported. Several clinical trials of medically ill hospitalized patients including a small proportion of patients with cancer have confirmed the efficacy of prophylactic anticoagulation in reducing the risk of VTE. These studies have demonstrated that enoxaparin (Medenox), dalteparin (Prevent) and fondaparinux (Artemis) are effective in the prevention of VTE detected on the basis of screening with venography or ultrasound.⁸⁻¹⁰ ASCO has recently developed clinical practice guidelines for the prevention and treatment of VTE in patients with cancer. These guidelines recommend consideration of

thromboprophylaxis in hospitalized patients with cancer and an extended course of anticoagulation after a VTE for 6 months or longer in patients with active malignancy.¹¹ VTE prophylaxis is not recommended in the ambulatory setting due to the lower risk of VTE and the recognition that patients with cancer are also at increased risk for major bleeding. As a result, recent studies have attempted to define clinical factors and biomarkers for identifying patients with cancer at increased risk for VTE who might benefit significantly from targeted thromboprophylaxis. A risk model for VTE in ambulatory patients with cancer receiving chemotherapy has recently been developed and validated.¹²

Despite strong and consistent guideline recommendations from ASCO, the American College of Chest Physicians, and the National Comprehensive Cancer Network favoring VTE prophylaxis in hospitalized patients with cancer, compliance with these recommendations has been suboptimal.^{13,14} As pointed out by Amin et al¹⁵ in this issue of *Journal of Oncology Practice*, hospitalized patients with cancer offered some type of prophylaxis may not be receiving the recommended full prophylactic dose and schedule of anticoagulation even after excluding patients considered low risk and those with contraindications to anticoagulation. These authors had previously reported that among 30,708 hospitalized cancer patients, 56% received some form of thromboprophylaxis. Only 28% received appropriate VTE prophylaxis. Eleven percent received only mechanical prophylaxis, and 16% received suboptimal doses or insufficient duration of anticoagulation.¹⁶ In the current expanded study of hospitalized patients with cancer receiving some type of VTE prophylaxis, fewer than 20% received thromboprophylaxis with the appropriate agent, doses, and duration on the basis of current guidelines. As noted by the authors, such suboptimal VTE prophylaxis was associated with increased risk of VTE, in-hospital mortality, and VTE readmission within 30 days of discharge. In addition, the average cost per discharge was higher among those receiving inadequate prophylaxis. Contraindications to anticoagulation in hospitalized patients with cancer, detailed in the ASCO Guidelines,¹¹ include active bleeding, aneurysms, severe hypertension, recent trauma, and epidural catheters, among others.¹¹ Nevertheless, no major bleeding or significant increase in minor bleeding was observed with appropriate VTE prophylaxis in this study. Although rates of use of VTE prophylaxis in hospitalized patients with cancer have improved, it is clear that there is much room for additional improvement.¹⁷⁻¹⁹

Clearly, the links between cancer and thrombosis have captured the interest of both oncologists and researchers.

Educational programs on cancer and thrombosis have been offered for the last 2 years at the Annual Meeting of ASCO, and a forthcoming issue of the *Journal of Clinical Oncology* will focus entirely on this topic. Through these efforts and those of other concerned professional organizations, further improvements in compliance with reasonable guideline recommendations for VTE prophylaxis in ill medical patients, including patients with cancer, should be observed. On the basis of retrospective data such as those presented here, improvements in compliance with VTE guidelines may result in lower rates of VTE, mortality, and early readmission for VTE without any escalation—and perhaps even a reduction—in associated health care costs.

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Authors' Disclosures of Potential Conflicts of Interest

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