



Venous thromboembolism in cancer patients: a call for more awareness

A. Delluc MD PhD and M. Carrier MD MSc†*

As elegantly reported by Drs. Shea–Budgell, Donnellan, and colleagues in the last issue of *Current Oncology*, venous thromboembolism (VTE) is a frequent clinical problem in cancer patients^{1,2}. Thromboembolism is the 2nd leading cause of death among cancer patients and dramatically worsens cancer prognosis^{3,4}. In cancer patients experiencing VTE, overall survival just a quarter of that experienced by cancer patients having the same tumour type and stage and receiving the same anticancer treatment, but not experiencing VTE complications. The increased overall mortality associated with VTE might be caused by postponed surgical procedures, delayed chemotherapies, VTE-related mortality (for example, fatal recurrent pulmonary embolism), or major bleeding caused by anticoagulant therapy. To prevent VTE in high-risk cancer patients, it is therefore important to increase clinical awareness among oncology health care professionals and to provide timely, effective treatment to patients with acute cancer-associated thrombosis.

To guide medical oncologists in the various management options for the prevention and treatment of VTE in cancer patients, clinical practice guidelines have been developed by the American Society of Clinical Oncology, the U.S. National Comprehensive Cancer Network, and the European Society of Medical Oncology^{5–7}. In their narrative review, Dr. Donnellan and colleagues summarized the rationale and key recommendations in the updated version of the American Society of Clinical Oncology's clinical practice guideline, enabling clinical application of the guideline in everyday practice¹. As emphasized in the review, cancer-specific data are available for some clinical indications (for example, pharmacologic thromboprophylaxis after cancer-related major abdominal surgery), but not for others (for example, pharmacologic thromboprophylaxis in hospitalized medically ill patients). In the latter cases, recommendations have to be based on extrapolations that use the reported high rates of efficacy and low rates hemorrhagic complications from clinical trials that included both cancer and non-cancer patients^{5,8}.

Given the known heightened risk for both VTE and major bleeding in cancer patients, further research is definitely needed to address these important knowledge gaps.

The evidence-based guidance from Dr. Shea–Budgell and colleagues goes further and also addresses the challenges encountered in the management of anticoagulation in cancer patients². As highlighted in their review, patients with cancer-associated thrombosis are more likely to experience recurrent VTE despite anticoagulation or to develop major bleeding episodes during anticoagulant therapy. Furthermore, cancer patients are more prone to undergo invasive procedures or to develop thrombocytopenia while anticoagulated, which might require temporary interruption of anticoagulant therapy and ultimately increase the risk of bleeding or recurrent VTE. Despite the lack of good-quality data supporting the various management options in these challenging clinical situations, the review by Dr. Shea–Budgell and colleagues provides much needed guidance to clinicians. The Scientific and Standardization Committee on Haemostasis and Malignancy of the International Society on Thrombosis and Haemostasis also developed expert consensus manuscripts that provide guidance about the various management options in these difficult but frequent clinical situations⁹. For example, it is suggested that, in cancer patients with symptomatic recurrent VTE despite anticoagulation with low molecular weight heparin, the heparin dose be increased by 20%–25%. Patients should be reassessed 5–7 days after dose escalation to ensure improvement of symptoms and good tolerance of the increased dose. Although these expert consensus recommendations are useful in managing difficult cases, their rationale is based on clinical expertise and small cohort studies^{10,11}. Large prospective studies are desperately needed to help tailor the recommendations concerning management of these frequent complications.

Venous thromboembolism is a frequent and clinically important issue in cancer patients. Clinical

practice guidelines and guidance are important to ensure proper prevention and treatment of VTE and to help manage anticoagulation challenges^{1,2}. However, more research is required to optimize prevention and to tailor management strategies in cancer-associated thrombosis.

CONFLICT OF INTEREST DISCLOSURES

The authors have no relevant conflicts of interest to declare.

REFERENCES

1. Donnellan E, Kevane B, Healey Bird BR Ni Ainle, F. Cancer and venous thromboembolic disease: from molecular mechanisms to clinical management. *Curr Oncol* 2014;21: 134-143 .
2. Shea-Budgell MA, Wu CMJ, Easaw JC on behalf of the Alberta Venous Thromboembolism Cancer Guideline Working Group. Evidence-based guidance on venous thromboembolism in patients with solid tumours. *Curr Oncol* 2014;21: e504-e514.
3. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. *J Thromb Haemost* 2007;5:632-4.
4. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. *Arch Intern Med* 2006;166:458-64.
5. Lyman GH, Khorana AA, Kuderer NM, *et al*. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2013;31:2189-204.
6. National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology: Venous Thromboembolic Disease*. Ver. 1.2011. Fort Washington, PA: NCCN; 2011. [Current version available online at: http://www.nccn.org/professionals/physician_gls/pdf/vte.pdf (free registration required); cited June 14, 2014]
7. Mandal M, Falanga A, Roila F on behalf of the ESMO Guidelines Working Group. Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines. *Ann Oncol* 2011;22(suppl 6):vi85-92.
8. Carrier M, Khorana AA, Moretto P, Le Gal G, Karp R, Zwicker JI. Lack of evidence to support thromboprophylaxis in hospitalized medical patients with cancer. *Am J Med* 2014;127:82-6.e1.
9. Carrier M, Khorana A, Zwicker J, Noble S, Lee A on behalf of the Subcommittee on Haemostasis and Malignancy for the SSC of the ISTH. Management of challenging cases of patients with cancer-associated thrombosis including recurrent thrombosis and bleeding: guidance from the SSC of the ISTH. *J Thromb Haemost* 2013;11:1760-5.
10. Carrier M, Le Gal G, Cho R, Tierney S, Rodger M, Lee AY. Dose escalation of low molecular weight heparin to manage recurrent venous thromboembolic events despite systemic anticoagulation in cancer patients. *J Thromb Haemost* 2009;7:760-5.
11. Ihaddadene R, Le GG, Delluc A, Carrier M. Dose escalation of low molecular weight heparin in patients with recurrent cancer-associated thrombosis. *Thromb Res* 2014;:[Epub ahead of print].

Correspondence to: Marc Carrier, The Ottawa Hospital Research Institute and University of Ottawa, 501 Smyth Road, Box 201A, Ottawa, Ontario K1H 8L6.

E-mail: mcarrier@ottawahospital.on.ca

* Département de Médecine Interne, University of Brest, Brest, France.

† Department of Medicine, The Ottawa Hospital Research Institute, University of Ottawa, Ottawa, ON.