

Hospital VTE Prevention Strategies for Cancer Patients

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Approximately 20% of all diagnosed VTE occur in individuals with cancer, involving 1/250 cancer patients annually. This likely represents an underestimation of actual VTE incidence since autopsy studies have indicated that over 50% of VTE in cancer patients are not appreciated or suspected antemortem. Epidemiologic studies have determined that cancer patients have a 6 fold higher incidence of VTE compared to the non CA population. The use of certain chemotherapeutic regimens, adjuvant therapies (such as SERMs and anti-angiogenic monoclonals), and erythropoietic growth factors can render malignancies not typically thought of as hypercoagulable states to become highly thrombogenic. A very good example of this is multiple myeloma treated with thalidomide or lenalidomide. A retrospective analysis of hospitalized Medicare patients in 1999 suggests that the survival of cancer patients with VTE is greatly truncated with less than 10% chance of surviving 6 months after discharge. This is in contrast to the 6 month post hospitalization likelihood of survival of non-CA patients with VTE alone (75%) or malignancy alone (around 65%). Symptomatic VTE is associated with a decreased survival in CA patients. Thus, there is rationale to anticoagulate medical CA patients to protect them from development of their first VTE. When it comes to surgery related VTE in CA patients, there are very robust data to indicate that VTE prophylaxis, maintained for up to 1 month post-operatively, effectively reduces the incidence of death by pulmonary embolism. Cancer patients have 2-fold risk of post-operative DVT/PE and >3-fold risk of fatal PE despite VTE prophylaxis.

ASCO guidelines from 2007 recommend that hospitalized patients with cancer should be considered candidates for VTE prophylaxis with anticoagulants in the absence of bleeding or other contraindications to anticoagulation. Similar recommendations have been developed by the ACCP (2008) and the NCCN (2008) guidelines at a grade 1A level, indicating definite benefit as derived from adequately powered, prospective, well conducted, randomized controlled clinical trials. Systemic VTE prophylaxis is usually accomplished by using LMWH or UFH unless there are contraindications to systemic anticoagulation when the use of mechanical means to prevent stasis can be implemented. Extrinsic pneumatic compression graduated support hose and the insertion of retrieval IVC filters, as the most feasible mechanical means, also can be used to enhance the VTE prophylaxis benefits of medical systemic approaches (Figure 1).

Guideline Recommendations

	Prophylaxis	When Anticoagulation Is Contraindicated
ASCO	UFH LMWH Fondaparinux	IPC GCS (IVC Filter?)
NCCN	UFH tid LMWH Fondaparinux	IPC GCS (IVC Filter?)
ACCP	UFH tid LMWH Fondaparinux (Grade 1A)	IPC GCS (IVC Filter?)

ASCO = American Society of Clinical Oncology; IPC = intermittent pneumatic compression; GCS = graduated compression stockings; IVC = inferior vena cava; NCCN = National Comprehensive Cancer Network; tid = 3 times daily; ACCP = American College of Chest Physicians.

Lyman GH, et al. J Clin Oncol. 2007;25:5490-5505. Geerts WH, et al. CHEST. 2008;133:381S-453S. NCCN. Venous Thromboembolic Disease v.1.2008. www.nccn.org/professionals/physician_gls/pdf/vte.pdf.

The data to support VTE prophylaxis in hospitalized CA patients are derived from much larger studies of medically ill patients, which included sizable cohorts of cancer patients. Despite this, compliance among physicians, and specifically oncologists, has been disappointingly low. There have been attempts to predict and stratify the risk levels of hospitalized CA patients who would be at greatest risk for developing VTE, recognizing that such patients may have other risk factors, which are conventionally recognized as adding risk potential for VTE, e.g. concurrent infection, age >60, BMI>30, immobility, etc. A recent study in which Caprini scores were calculated for each CA patient (Abdel-Razeq, JTH, 2010) suggests that low risk CA patients may not require VTE prophylaxis although the VTE incidence for high risk CA hospitalized patients was 4.2%.

So why is there such poor compliance for VTE prophylaxis in the medically ill hospitalized CA patient? Several explanations have been offered, including the fact that oncologists do not consider VTE to be a major complication of their overall delivered care; the fact that the ability and expense to achieve extended VTE prophylaxis in the CA patient using LMWH is complicated by Medicare and insurance restrictions against the use of outpatient parenteral medications; that the use of ongoing anticoagulation is rendered more difficult in the CA patient receiving chemotherapy because of attending thrombocytopenia; and that patients are not sufficiently aware of the risks of developing VTE complications to demand prophylaxis measures of their oncologists.

Numerous strategies have been utilized to encourage oncologists to implement VTE prophylaxis in their CA patients with variable success. Even the computer-based approaches, which force the physician to opt out of VTE anticoagulation have indicated lowest compliance in cancer patients. It is apparent that even in the world's best hospitals which advocate VTE prophylaxis according to ACCP/NCCN/ASCO guidelines come up short on CA patient implementation of VTE prophylactic regimens. When considering the best approaches to VTE prophylaxis for hospitalized CA patients, which might improve compliance, the following thoughts are offered:

- 1) US cancer patients receiving partial, inadequate or no prophylaxis have a higher risk of VTE and mortality than patients receiving full guideline-recommended prophylaxis, leading to a higher total hospital cost. It may be that hospitals will insist on VTE prophylaxis for all CA patients unless there is major risk to implement. (Amin et al. ASH, 2009, abstract 169).
- 2) Perhaps the best approach to implement VTE prophylaxis in the hospitalized CA patient is to educate hospitalists, rather than to depend on the oncologist.
- 3) Another approach may be to include VTE prophylaxis on the palliative care menu for hospitalized CA patients. MSW help may be able to facilitate outpatient continuity.
- 4) The introduction of biosimilar LMWH may lower the cost of outpatient continuity of VTE prophylaxis in the CA patient. The future introduction of oral direct anti-Xa and oral anti-IIa agents which will circumvent the need for parenteral administration and the need for INR monitoring if warfarin were contemplated.
- 5) Increase the education level of CA patients about VTE risks so that they will demand VTE risk reduction measures from their health care providers.