Long-Term Therapy of Venous Thromboembolism in Cancer Patients

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Key Words
Venous thromboembolism, deep vein thrombosis, pulmonary embolism, cancer, anticoagulation, low molecular weight heparin, vitamin K antagonist

Abstract
Venous thromboembolism (VTE) is a common complication in cancer patients that results in significant morbidity and mortality. Long-term treatment options for cancer patients who experience VTE include vitamin K antagonists (VKAs), low molecular weight heparins (LMWHs), and inferior vena caval (IVC) filters. Cancer patients have a two- to fourfold higher risk for experiencing recurrent VTE and major bleeding during chronic VKA therapy than patients without malignancies. Recent randomized clinical trials have shown that LMWHs rather than oral VKAs are preferred for initial chronic treatment of VTE in patients with advanced cancer. One factor potentially limiting the broader use of LMWH for chronic therapy in the United States is its higher acquisition cost. Efficacy, cost, drug availability, patient comorbidities, and concomitant medications all need to be considered when selecting chronic VTE therapy. Cancer patients with VTE should be treated for as long as their disease is active to minimize the incidence of recurrence. Use of IVC filters should generally be reserved for patients at high risk for recurrent VTE who have contraindications to anticoagulation. Several new anticoagulants are being investigated that promise greater therapeutic choices and potentially better outcomes for cancer patients with VTE. (JNCCN 2006;4:903–910)

Epidemiology
Venous thromboembolism (VTE) is a frequent occurrence in cancer patients. The annual incidence of VTE is approximately 5 times more common among cancer patients (0.5%) than the general population (0.1%). Among cancer patients, 15% experience a thromboembolic event during their clinical course, and autopsy studies indicate that as many as 50% have evidence of VTE on postmortem examination. VTE has significant clinical consequences for cancer patients: it increases mortality risk by threefold and may be responsible for 14% of deaths in hospitalized cancer patients. Consequently, prevention and treatment of VTE are important components of therapy for patients with malignancies.

Etiology
The etiology of the hypercoagulable state associated with cancer is multifactorial and tightly linked with the growth and metastasis of the disease. Tumor cells have been shown to express procoagulant proteins, such as tissue factor and cancer procoagulant, that activate the coagulation cascade. Tissue factor and thrombin induce vascular endothelial growth factor expression, a key regulator of angiogenesis that promotes new vessel growth and induces further tissue factor expression, establishing a vicious cycle of neoangiogenesis and hypercoagulability. Cancer cells also activate host monocytes, endothelial cells, and platelets that contribute to the procoagulant state by expressing tissue factor or releasing adhesive proteins such as von Willebrand factor and fibrinogen.

The inflammatory state induced by cancer also contributes to the milieu of hypercoagulability by increasing the expression of acute-phase reactants, such as von Willebrand factor, factor VIII, and fibrinogen. Fibrin and activated platelet aggregates induced by thrombin generation contribute to metastasis by binding to intravascular cancer cells and forming protective cocoons that shield them from immune recognition and promote endothelial binding at distant sites, thereby establishing

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Cancer cells also contribute to new foci of disease.\textsuperscript{7–9} Cancer cells also contribute to thrombosis through local effects by compressing vessels and slowing blood flow. Immobility caused by reduced performance status and the neurologic consequences of central nervous system disease also help lead to the high incidence of VTE in cancer patients. Clinical studies indicate that cancer therapies, including surgery, chemotherapy, and radiation therapy, play a role in the development of thrombotic events and contribute to the increased risk for VTE in cancer patients.\textsuperscript{10–13}

**Goals of Long-Term Management of VTE**

The goal of chronic anticoagulation is to suppress the coagulation mechanism, thereby arresting thrombus progression and preventing further episodes of thromboembolism. By preventing further accumulation of thrombus, chronic anticoagulation allows the endogenous fibrino-lytic machinery to reduce the existing clot burden and perhaps preserve valvular function. Traditionally, oral vitamin K antagonists (VKAs) and, to a lesser extent, inferior vena caval (IVC) filters have been used to accomplish these goals. More recently, low molecular weight heparin (LMWH) has been used in the chronic management of VTE in cancer patients. This article reviews the data supporting the usefulness of these management options.

**Vitamin K Antagonists**

**Mechanism of Action**

VKAs, such as warfarin, have been used in the chronic treatment of VTE for more than 5 decades. VKAs produce their anticoagulant effect by disrupting vitamin K metabolism in the liver. VKAs inhibit enzymes such as vitamin K epoxide reductase and, to a lesser extent, vitamin K reductase, creating a deficiency of reduced vitamin K\textsubscript{1} in the liver. In the absence of this critical cofactor, the post-translational addition of gamma carboxy-glutamic acid side chains to the vitamin K–dependent factors II (prothrombin), VII, IX, and X, and the endogenous anticoagulant proteins C and S, are blocked. Without these side chains, these coagulation factors cannot bind to phospholipid-rich membranes (e.g., the surface of activated platelets) and therefore cannot function as effective procoagulant (e.g., factors II, VII, IX, X) or anticoagulant (e.g., protein C, protein S) proteins.\textsuperscript{14} VKAs inhibit the production of functional forms of these coagulation proteins rather than directly inhibiting their activity in the blood. Consequently, their anticoagulant effect has a gradual onset that corresponds to the plasma half-life of the vitamin K–dependent coagulation factors. Because the most important procoagulant proteins, factors II and X, have prolonged half-lives (72 and 36 hours, respectively) compared with the anticoagulant protein C (approximately 10 hours), VKA therapy, particularly when initiated with loading doses, can be associated with a transient period of hypercoagulability owing to the more rapid decline in functional protein C compared with the longer-lived procoagulant factors II and X. Consequently, VKAs in acute therapy for VTE are always initiated with rapid-onset anticoagulants, such as unfractionated heparin (UFH), LMWH, or fondaparinux.\textsuperscript{14}

**Characteristics and Clinical Results in Cancer Patients**

As chronic therapeutic agents for VTE, VKAs have several advantages, including oral administration and a long half-life. The latter feature means that missed doses will not be accompanied by significant declines in drug concentrations and anticoagulant activity, which might precipitate recurrent episodes of thromboembolism. In addition, the effect of VKAs can be easily reversed by administering vitamin K\textsubscript{1} or blood products, such as fresh frozen plasma or prothrombin complex concentrates.

VKAs also have several disadvantages, including a narrow therapeutic window, substantial interindividual differences in dose response, and significant potential for dietary and drug-to-drug interactions. Consequently, anticoagulation intensity must be closely monitored to prevent recurrent thromboembolism or anticoagulant-associated bleeding. The long half-life of VKAs can also complicate anticoagulation management in response to thrombocytopenia or invasive procedures.\textsuperscript{14}

Despite these shortcomings, the results of chronic VKA therapy in the general population of patients with VTE have been favorable. The incidence of recurrent VTE and major bleeding in randomized clinical trials of chronic VKA therapy each have been as low as 1 episode per 100 person-years.\textsuperscript{15} In contrast, clinical results in cancer patients have been less encouraging. In a retrospective review of their experience with recurrent thromboembolism, Bona
et al.\textsuperscript{16} noted a sixfold difference in incidence between cancer patients (0.013 episodes per patient month) and non-cancer patients (0.002 episodes per patient month). Several large cohort studies and a retrospective analysis of 2 randomized clinical trials of anticoagulation have confirmed these results.

In a retrospective analysis of the Italian Study of Complications of Oral Anticoagulant Treatment (ISCOAT), Palareti et al.\textsuperscript{17} noted recurrent VTE in 6.8% of cancer patients (n = 95) versus 2.5% in patients without malignancies (n = 828; P = .058). Despite similar-quality anticoagulant therapy (time in therapeutic range approximately 70% in both groups), major bleeding was more frequent in patients with cancer than in those without (5.4% vs. 0.9%; P = .0019). In contrast to patients without malignancies, whose bleeding complications were primarily associated with elevated international normalized ratio (INR) values, cancer patients experienced increased rates of bleeding in all INR categories.

Hutten et al.\textsuperscript{18} noted similar results in their analysis of the Tasman and Columbus studies, 2 randomized clinical trials comparing LMWH with UFH for VTE treatment. Cancer patients were 3 times more likely to experience recurrent VTE (27.1 vs. 9.0 per 100 patient years; P = .003) and 6 times more likely to experience major bleeding (13.3 vs. 2.1 per 100 patient years; P = .002) than patients without cancer. Among both groups of patients, recurrent VTE was highest when the INR was below 2. Paradoxically, bleeding complications occurred more often in cancer patients at subtherapeutic INR values. This finding emphasizes the importance of non-anticoagulation-associated factors (e.g., thrombocytopenia, vascular invasion) in bleeding among cancer patients.

Prandoni et al.\textsuperscript{19} also noted the adverse clinical course of cancer patients with VTE. They analyzed a prospective cohort of 842 patients with VTE in which 181 had cancer and 67 (37%) had advanced disease (TNM stage IV). The 12-month cumulative incidences of VTE (20.7% vs. 6.8%) and major bleeding (12.4% vs. 4.9%) were 3.2 times (95% confidence interval [CI], 1.9–5.4) and 2.2 times (95% CI, 1.2–4.1) higher in cancer patients than in those without malignancies, respectively. Recurrent VTE and major bleeding in cancer patients were more frequent during the first month of therapy and occurred more often in patients with extensive disease. Bleeding was not associated with the level of anticoagulation.

Potential strategies to improve the results of VKA therapy in cancer patients include increasing the frequency of INR monitoring and using specialized anticoagulation clinics to manage therapy. Previous studies have shown that these strategies are associated with increased time spent in the therapeutic range compared with usual care.\textsuperscript{14} However, data from the studies described previously suggest that these approaches will not eliminate the disparate outcomes of cancer patients.\textsuperscript{17–19} Despite spending a similar percentage of time in the therapeutic range, cancer patients in the ISCOAT study showed inferior outcomes.\textsuperscript{15} Hutten et al.\textsuperscript{18} and Prandoni et al.\textsuperscript{19} both noted more episodes of VTE and major bleeding among cancer patients irrespective of INR level. In addition, the time in therapeutic range noted by Prandoni et al.\textsuperscript{19,20} and the ISCOAT\textsuperscript{15,17} study was comparable to the best results obtained in randomized controlled trials of VKA therapy. Therefore, improved management of VKA therapy is unlikely to substantially improve the results of chronic anticoagulation in cancer patients.

**Inferior Vena Caval Filters**

Increased use of IVC filters to manage VTE in cancer patients is another potential way to reduce the adverse effects of VKA therapy. Several early case series suggested that anticoagulation in cancer patients was associated with a high frequency of major bleeding events (20%–50%) and proposed that vena caval filters should be considered the preferred form of therapy for VTE in this patient population.\textsuperscript{21,22} However, comparative case series of cancer patients treated with IVC filters or anticoagulation indicate that those treated with filters experienced more symptomatic episodes of DVT, pulmonary embolism, and IVC thrombosis than those undergoing anticoagulation. In addition, applying filters to VTE in cancer patients was not associated with a survival advantage.\textsuperscript{23,24}

Although case series data have significant weaknesses, these conclusions are plausible given that the PREPIC study found a significant increase in recurrent DVT and no impact on mortality associated with filter placement after 8 years of follow-up.\textsuperscript{25} Population-based observational studies have found similar results.\textsuperscript{26}

Because IVC filters provide no therapy for the underlying thrombotic process, these devices should be
reserved for patients with acute thrombosis who have a high risk for thromboembolism and a contraindication to anticoagulation. Although retrievable IVC filters may offer an attractive option for patients with temporary contraindications to anticoagulation, preliminary experiences indicate that many filters are not retrieved, and whether retrievable filters function as well as permanent IVC filters has not been determined.27

LMWH

Because of the limitations of traditional approaches, interest in using LMWHs for the chronic treatment of VTE in cancer patients has increased. LMWHs are derived from chemical or enzymatic depolymerization of porcine UFH, resulting in an average molecular weight between 4500 and 7500 daltons for LMWH compared with a mean molecular weight of 15,000 daltons for UFH. Because of its lower molecular weight and shorter average polysaccharide chain length, LMWH is much less likely to bind to plasma proteins and cell membranes, and there is a longer plasma half-life and more predictable pharmacokinetics than UFH. LMWH is also less likely to cause heparin-induced thrombocytopenia (HIT) and osteoporosis.

Similar to UFH, LMWH exerts its antithrombotic effect by binding to antithrombin (AT) and causing a conformational change that accelerates AT's inhibition of activated factors X (factor Xa) and II (thrombin). The smaller chain lengths of LMWH are less able to coordinate the inhibitory interaction between thrombin and AT, and therefore the LMWH–AT complex has disproportionately greater inhibitory activity against factor Xa than UFH.28

Although there is a tendency to use LMWHs as if they have uniform pharmacologic and clinical properties, each has a different manufacturing process, molecular weight, and Xa:IIa inhibitory ratio.29 While one recent randomized clinical trial showed equivalent clinical outcomes for tinzaparin and dalteparin in the acute treatment of VTE, additional studies are warranted before LMWHs can be considered interchangeable.30

The pharmacologic properties of LMWHs give them several advantages over VKAs for long-term treatment of VTE. LMWHs are not affected by changes in diet or medications and have short half-lives.28 The latter characteristic is particularly attractive for cancer patients, who often experience thrombocytopenia and the need for invasive procedures that require transient interruptions in therapy. Several randomized clinical trials have suggested that LMWHs are a viable alternative to VKAs in the chronic treatment of VTE. However, because only a few of the patients had cancer,31-33 these studies did not provide sufficient evidence to support the use of LMWH in these patients.

LMWH Versus VKA for the Chronic Treatment of VTE

Several randomized clinical trials have investigated the effectiveness of LMWH for the chronic treatment of VTE in cancer patients. CATHANOX was the first published trial of LMWH and VKA in cancer patients, which compared 3 months of warfarin (INR 2–3) with a once-daily dose of enoxaparin, 1.5 mg/kg.34 Cancer patients planning to undergo surgery or chemotherapy with a high potential to cause severe thrombocytopenia were excluded. Because of slow accrual, the study was closed prematurely after enrolling 146 of 240 (62%) subjects. At enrollment, 53% of the participants had metastatic cancer and 72% were undergoing active treatment of their cancer.

Of the patients treated with warfarin, 15 (21.2%) experienced an episode of VTE or major bleeding compared with 7 patients (10.5%) treated with enoxaparin (P = .09). During the 3-month study, 17 patients (22.7%) treated with warfarin and 8 patients (11.3%) treated with enoxaparin died (P = .07). Fatal hemorrhages occurred in 6 patients treated with warfarin, whereas none occurred in those treated with enoxaparin. Despite a mean frequency of INR measurements of 2.4 per week in the warfarin group, the percentage of time in the therapeutic range was only 41%.34

The ONCENOX study compared enoxaparin with warfarin in cancer patients.35 This 3-arm study randomized 102 patients to undergo treatment with 2 different enoxaparin doses (1.5 mg/kg/d or 1 mg/kg/d) or warfarin (INR 2–3) for 180 days. Only 3.3% of patients treated with enoxaparin experienced recurrent VTE compared with 6.7% of patients treated with warfarin. Similar to the CATHANOX study, these results were not statistically significant because of the limited number of subjects. Further details will be available when the results are published.
The LITE study investigated tinzaparin as an alternative to warfarin for the secondary prevention of VTE. This randomized clinical trial compared 3 months of tinzaparin monotherapy with UFH followed by warfarin (INR 2–3) in 737 patients with proximal DVT, 206 (28%) of which had cancer. Recurrent VTE occurred in 6 patients treated with tinzaparin (5.9%) and 11 treated with warfarin (10.5%; 95% CI, −12% to 2.9%; P = not significant). Although these results are limited by the fact that this was a subgroup analysis and that acute therapy differed between the groups, they provide preliminary evidence that tinzaparin is a viable alternative to warfarin for chronic treatment of VTE in cancer patients.6

The results of the CLOT trial provide the strongest evidence for the use of LMWH as chronic therapy for VTE in cancer patients. Lee et al. randomized 676 cancer patients with VTE to 6 months of treatment with dalteparin or VKA adjusted to achieve an INR of 2 to 3. Eligible patients had active cancer, an Eastern Cooperative Oncology Group (ECOG) performance status of 1 or 2, and an objectively documented VTE. Patients with high risk for bleeding were excluded. Of 1303 cancer patients presenting with VTE, 676 were enrolled in the study. Among these participants, 90% had solid tumors and 67% had metastatic disease.

Patients treated with dalteparin received 200 IU/kg once daily for the first month, followed by 150 IU/kg for months 2 through 6. Patients treated with VKA underwent acute treatment with once-daily dalteparin, 200 IU/kg, for at least 5 to 7 days until their INR reached 2 or more on 2 consecutive days, after which they were treated with INR-adjusted VKA therapy. INR measurements were performed at least every 2 weeks. Patients treated with VKA were in the therapeutic range 46% of the time. Recurrent VTE occurred in 27 patients treated with dalteparin (9%) and 53 patients treated with VKA (17%), for a VTE hazard ratio of 0.48 (95% CI, 0.30–0.77; P = .002). In the warfarin group, 20 of 53 recurrent VTE (38%) episodes occurred when the INR was less than 2. Major bleeding (dalteparin, 6% vs. VKA, 4%; P = .27) and 6-month mortality rates (dalteparin, 39% vs. VKA, 41%; P = .57) were similar in both groups. Among the deaths, 90% were caused by progressive cancer.

Each study has several limitations. All were open randomized studies because double-blind randomized clinical trials would have been extremely difficult to execute safely in this population. Although outcome events were assessed using a prespecified protocol in some cases, and all studies used an independent masked adjudication committee to review events, open trials are subject to diagnostic suspicion bias that can influence outcomes. In addition, the warfarin control was suboptimal time in therapeutic ranges, 41% and 46%, respectively, in the 2 studies reporting data for this measure compared with other studies in cancer patients. However, dissimilar patient populations may also be responsible for these different results.

Finally, because only one third of patients eligible for the 2 studies were enrolled, these results may not apply to all cancer patients. Nevertheless, the combined results of these studies warrant serious consideration of LMWH for any patient with advanced cancer who experiences VTE. These data prompted the 7th American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy to recommend LMWH as the preferred approach to the chronic treatment of VTE in cancer patients for at least the first 3 to 6 months of therapy.

Another important consideration when choosing chronic therapy for VTE in cancer patients is cost. Although initial outpatient therapy with LMWH has been shown to be cost-effective compared with UFH, chronic LMWH therapy is significantly more expensive than VKA therapy. A recent decision analysis found that although LMWH resulted in an average increased quality-adjusted life-expectancy surplus of 19 days, it cost an additional $7609 per patient treated. Therefore, physicians and cancer patients must carefully weigh the greater efficacy and cost of LMWH when deciding on secondary prevention of VTE. Patient preferences, current drug therapy; comorbidities, and drug acquisition cost must be considered.

The benefits of LMWH could be maximized by using it mainly in patients with the highest risk for VKA-associated complications, such as those with advanced disease or poor hepatic function. Another strategy would be to use LMWH preferentially in the first 3 months of therapy when the risk for recurrent VTE is highest.

**Duration of Therapy for VTE in Cancer Patients**

Cancer and its treatment are associated with a significant and persistent risk for recurrent VTE. Consequently, therapy for VTE in cancer patients should continue for as long as the cancer is active.
If the patient is disease-free, then therapy should continue for a period appropriate to the patient’s specific thrombotic event. For an initial extremity deep vein thrombosis (including calf deep veins) associated with a major transient risk factor (e.g., major surgery, trauma), at least 3 months of therapy is appropriate. Most patients experiencing a pulmonary embolism associated with a transient risk factor should undergo at least 6 months of therapy given the higher case fatality rate associated with recurrent pulmonary embolism.

For idiopathic VTE, at least 6 to 12 months of therapy are recommended. Because indefinite therapy has been associated with the best clinical outcomes for patients with idiopathic VTE, this approach should be considered in patients likely to benefit from longer therapy (e.g., compliant, no risk factors for bleeding). Patients with a second episode of VTE or a first episode associated with significant thrombophilic defects (e.g., antiphospholipid syndrome, homozygous factor V Leiden, combined heterozygosity for factor V Leiden and the prothrombin gene mutation, deficiency of antithrombin, protein C or protein S) should also be considered for long-term anticoagulation. Because heterozygosity for factor V Leiden or the prothrombin gene mutation is not associated with a substantially increased risk for recurrent VTE, the presence of these abnormalities in isolation does not warrant extension of therapy.

A significant percentage of cancer patients have central venous catheters for phlebotomy and administering chemotherapy and blood products. Prospective studies indicate that symptomatic catheter-associated deep vein thrombosis affects 1% to 26% of cancer patients with a central venous catheter. Although no trials have examined the duration of therapy for catheter-associated deep vein thrombosis, treating these events similar to triggered lower extremity deep vein thrombosis seems reasonable. Treatment should continue for at least 3 months or the duration of the catheter, whichever is longer. To prevent post-thrombotic symptoms, all cancer patients with deep vein thrombosis should be prescribed compression stockings (30–40 mm Hg).

Management of Recurrent VTE
Cancer patients have a high incidence of recurrent VTE. Patients with recurrent VTE should be managed based on their particular clinical situation. For patients undergoing VKA therapy who experience a recurrence in the setting of a subtherapeutic INR, targeting VKA therapy to a higher INR range (2.5–3.5) after acute therapy with UFH or LMWH is one reasonable option. Alternatively, chronic LMWH therapy could be considered, particularly if VKA control was suboptimal. One study noted a low recurrence rate in patients treated with LMWH in this situation.

In patients who experience recurrence despite therapeutic anticoagulation with a VKA, long-term LMWH therapy is strongly recommended because little information supports the effectiveness of high-intensity VKA therapy (INR 3–4) in cancer patients. Although recurrent VTE during LMWH therapy is less common, when it occurs, clinicians must objectively document recurrent thrombosis and establish whether noncompliance or inadequate dosing may have contributed to the event. At least one study of enoxaparin in cancer patients documented an increased risk for recurrence with once-daily therapy. Therefore, any patient who experiences a recurrent thrombotic event during enoxaparin therapy should undergo twice-daily therapy (1 mg/kg subcutaneously every 12 hours). Rarely, patients with Trousseau syndrome will experience resistance to LMWH. Continuous-infusion UFH therapy has been effective in preventing further thrombotic events in these patients (unpublished observations). Other important causes of recurrent thromboembolism in cancer patients include HIT and anatomic causes, such as direct vascular compression. Using appropriate diagnostic testing to identify these syndromes is critical to avert additional episodes of thromboembolism.

Vena caval filters are commonly recommended for treating recurrent VTE, despite adequate anticoagulation. However, they should be used sparingly in cancer patients for several reasons. Retrospective cohort studies have noted that recurrent thromboembolism has led to inferior outcomes with vena caval filters. These results in cancer patients are similar to those of the PREPIC study. The hypercoagulable state associated with cancer affects all vascular beds. Therefore, regional approaches to VTE (e.g., filters) are unlikely to provide significant additional protection without concomitant aggressive systemic anticoagulation, and may compromise rather than enhance the results.
New Anticoagulants

Fondaparinux is a synthetic indirect factor Xa inhibitor that has shown efficacy in preventing and treating VTE. Similar to LMWH, fondaparinux is administered subcutaneously in once-daily weight-based doses. It has a half-life of 17 to 21 hours and is cleared renally. Unlike heparins, fondaparinux has not been associated with the development of HIT and has been used to successfully treat patients with this condition. Therefore, fondaparinux may be useful in the chronic management of VTE in cancer patients.

Several other factor Xa inhibitors are in various stages of drug development, including idraparinux, which is a long-acting indirect factor Xa inhibitor similar to fondaparinux, and rivaroxaban, which is an oral direct factor Xa inhibitor. Although the future availability of ximelgatran in the United States remains unclear, another oral thrombin inhibitor, dabigatran, is currently in clinical development. The large number of new antithrombotics currently being investigated portends a brighter future for cancer patients experiencing VTE.

Summary

VTE is a common complication in cancer patients that results in significant morbidity and mortality. An evidence-based approach to management is essential for optimal patient outcomes. Recent studies indicate that LMWHs, rather than oral VKAs, are preferred for initial chronic therapy (during the first 3–6 months) for VTE in patients with advanced cancer. One factor potentially limiting the broader use of LMWH for chronic therapy in the United States is its higher acquisition cost. Although one clinical trial showed no significant differences in patient outcome between 2 different LMWHs, no studies have shown that all LMWHs are pharmacologically interchangeable. Therefore, efficacy, cost, availability, patient comorbidities, and concomitant medications should all be considered when selecting chronic VTE therapy.

Cancer patients with VTE should be treated for as long as their cancer is active to minimize recurrent events. IVC filters generally should only be used in patients at high risk for recurrent VTE who have contraindications to anticoagulation. Broader use of filters (e.g., anticoagulation failure) should be used very selectively. LMWH should be strongly considered for cancer patients with recurrent VTE. HIT and anatomic factors must be considered when evaluating cancer patients with recurrent VTE. Several new anticoagulants are currently being investigated that promise greater therapeutic choices and better outcomes for cancer patients with VTE.

References


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