guideline summaries

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update Summary

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Venous thromboembolism (VTE), which includes deep vein thrombosis and pulmonary embolism, is an important cause of morbidity and mortality among patients with cancer.[1,2] Patients with cancer are significantly more likely to develop VTE than people without cancer[3] and experience higher rates of VTE recurrence and bleeding complications during VTE treatment.[4,5]

Comprehensive management of VTE in patients with cancer includes both the identification of patients who are most likely to benefit from pharmacologic prophylaxis, as well as effective treatment to reduce the risk of VTE recurrence and mortality. ASCO first published a guideline on these topics in 2007,[6] with updates in 2013[7] and 2015.[8] The 2015 update reaffirmed the 2013 recommendations. The current update revises several previous recommendations. Most notably, direct oral anticoagulants have been added as options for VTE prophylaxis and treatment. Additional information is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.

WHAT IS PRACTICE CHANGING

Changes to previous recommendations: clinicians may offer thromboprophylaxis with apixaban, rivaroxaban, or low-molecular-weight heparin to selected high-risk outpatients with cancer; rivaroxaban and edoxaban have been added as options for VTE treatment; patients with brain metastases are now addressed in the VTE treatment section; and the recommendation regarding long-term postoperative low-molecular-weight heparin has been expanded.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

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THE BOTTOM LINE

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update

Guideline Question

How should venous thromboembolism (VTE) be prevented and treated in patients with cancer?

Target Population

Adults with cancer.

Target Audience

Oncologists, surgeons, oncology nurses, oncology pharmacists, other health care professionals who care for patients with cancer, patients, and caregivers.

Methods

An Expert Panel was convened to update clinical practice guideline recommendations based on a systematic review of the medical literature.

Recommendations

Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?

Recommendation 1.1. Hospitalized patients who have active malignancy and acute medical illness or reduced mobility should be offered pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 1.2. Hospitalized patients who have active malignancy without additional risk factors may be offered pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications (Type: evidence based; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 1.3. Routine pharmacologic thromboprophylaxis should not be offered to patients admitted for the sole purpose of minor procedures or chemotherapy infusion, nor to patients undergoing stem-cell/bone marrow transplantation (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?

Recommendation 2.1. Routine pharmacologic thromboprophylaxis should not be offered to all outpatients with cancer (Type: evidence based; Evidence quality: intermediate to high; Strength of recommendation: strong).

Recommendation 2.2. High-risk outpatients with cancer (Khorana score of 2 or higher prior to starting a new systemic chemotherapy regimen) may be offered thromboprophylaxis with apixaban, rivaroxaban, or low-molecular-weight heparin (LMWH) provided there are no significant risk factors for bleeding and no drug interactions. Consideration of such therapy should be accompanied by a discussion with the patient about the relative benefits and harms, drug cost, and duration of prophylaxis in this setting (Type: evidence based; Evidence quality: intermediate to high for apixaban and rivaroxaban, intermediate for LMWH; Strength of recommendation: moderate).

Recommendation 2.3. Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone should be offered pharmacologic thromboprophylaxis with either aspirin or LMWH for lower-risk patients and LMWH for higher-risk patients (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).

Should patients with cancer undergoing surgery receive peri-operative VTE prophylaxis?

Recommendation 3.1. All patients with malignant disease undergoing major surgical intervention should be offered pharmacologic thromboprophylaxis with either unfractionated heparin (UFH) or LMWH unless contraindicated because of active bleeding, or high bleeding risk, or other contraindications (Type: evidence based; Evidence quality: high; Strength of recommendation: strong).

Recommendation 3.2. Prophylaxis should be commenced preoperatively (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

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Recommendation 3.3. Mechanical methods may be added to pharmacologic thromboprophylaxis but should not be used as monotherapy for VTE prevention unless pharmacologic methods are contraindicated because of active bleeding or high bleeding risk (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 3.4. A combined regimen of pharmacologic and mechanical prophylaxis may improve efficacy, especially in the highest-risk patients (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 3.5. Pharmacologic thromboprophylaxis for patients undergoing major surgery for cancer should be continued for at least 7 to 10 days. Extended prophylaxis with LMWH for up to 4 weeks postoperatively is recommended for patients undergoing major open or laparoscopic abdominal or pelvic surgery for cancer who have high-risk features such as restricted mobility, obesity, or history of VTE, or with additional risk factors. In lower-risk surgical settings, the decision on appropriate duration of thromboprophylaxis should be made on a case-by-case basis (Type: evidence based; Evidence quality: high; Strength of recommendation: moderate to strong).

What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?

Recommendation 4.1. Initial anticoagulation may involve LMWH, UFH, fondaparinux, or rivaroxaban. For patients initiating treatment with parenteral anticoagulation, LMWH is preferred over UFH for the initial 5 to 10 days of anticoagulation for the patient with cancer with newly diagnosed VTE who does not have severe renal impairment (defined as creatinine clearance < 30 mL/min; Type: evidence based; Evidence quality: high; Strength of recommendation: strong).

Recommendation 4.2. For long-term anticoagulation, LMWH, edoxaban, or rivaroxaban for at least 6 months are preferred because of improved efficacy over vitamin K antagonists (VKA). VKA are inferior, but may be used if LMWH or direct oral anticoagulants (DOAC) are not accessible. There is an increase in major bleeding risk with DOAC, particularly observed in GI and potentially genitourinary malignancies. Caution with DOAC is also warranted in other settings with high risk for mucosal bleeding. Drug-drug interaction should be checked prior to using a DOAC (Type: evidence based; Evidence quality: high; Strength of recommendation: strong).

Recommendation 4.3. Anticoagulation with LMWH, DOAC, or VKA beyond the initial 6 months should be offered to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy. Anticoagulation beyond 6 months needs to be assessed on an intermittent basis to ensure a continued favorable risk-benefit profile (Type: informal consensus; Evidence quality: low; Strength of recommendation: weak to moderate).

Recommendation 4.4. Based on expert opinion in the absence of randomized trial data, uncertain short-term benefit, and mounting evidence of long-term harm from filters, the insertion of a vena cava filter should not be offered to patients with established or chronic thrombosis (VTE diagnosis more than 4 weeks ago) nor to patients with temporary contraindications to anticoagulant therapy (eg, surgery). There also is no role for filter insertion for primary prevention or prophylaxis of pulmonary embolism (PE) or deep vein thrombosis due to its long-term harm concerns. It may be offered to patients with absolute contraindications to anticoagulant therapy in the acute treatment setting (VTE diagnosis within the past 4 weeks) if the thrombus burden was considered life-threatening. Further research is needed (Type: informal consensus; Evidence quality: low to intermediate; Strength of recommendation: moderate).

Recommendation 4.5. The insertion of a vena cava filter may be offered as an adjunct to anticoagulation in patients with progression of thrombosis (recurrent VTE or extension of existing thrombus) despite optimal anticoagulant therapy. This is based on the panel's expert opinion given the absence of a survival improvement, a limited short-term benefit, but mounting evidence of the long-term increased risk for VTE (Type: informal consensus; Evidence quality: low to intermediate; Strength of recommendation: weak).

Recommendation 4.6. For patients with primary or metastatic central nervous system malignancies and established VTE, anticoagulation as described for other patients with cancer should be offered, although uncertainties remain about choice of agents and selection of patients most likely to benefit (Type: informal consensus; Quality of evidence: low; Strength of recommendation: moderate).

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Recommendation 4.7. Incidental PE and deep vein thrombosis should be treated in the same manner as symptomatic VTE, given their similar clinical outcomes compared with patients with cancer with symptomatic events (Type: informal consensus; Evidence quality: low; Strength of recommendation: moderate).

Recommendation 4.8. Treatment of isolated subsegmental PE or splanchnic or visceral vein thrombi diagnosed incidentally should be offered on a case-by-case basis, considering potential benefits and risks of anticoagulation (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?

Recommendation 5. Anticoagulant use is not recommended to improve survival in patients with cancer without VTE (Type: evidence based; Evidence quality: high; Strength of recommendation: strong).

What is known about risk prediction and awareness of VTE among patients with cancer?

Recommendation 6.1. There is substantial variation in risk of VTE between individual patients with cancer and cancer settings. Patients with cancer should be assessed for VTE risk initially and periodically thereafter, particularly when starting systemic antineoplastic therapy or at the time of hospitalization. Individual risk factors, including biomarkers or cancer site, do not reliably identify patients with cancer at high risk of VTE. In the ambulatory setting among patients with solid tumors treated with systemic therapy, risk assessment can be conducted based on a validated risk assessment tool (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 6.2. Oncologists and members of the oncology team should educate patients regarding VTE, particularly in settings that increase risk such as major surgery, hospitalization, and while receiving systemic antineoplastic therapy (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: strong).

Notes regarding off-label use in guideline recommendations: apixaban, rivaroxaban, and LMWH have not been approved by the Food and Drug Administration for thromboprophylaxis in outpatients with cancer (recommendation 2.2 for apixaban and rivaroxaban; recommendations 2.2 and 2.3 for LMWH). Dalteparin is the only LMWH with Food and Drug Administration approval for extended therapy to prevent recurrent thrombosis in patients with cancer (recommendation 4.2).

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

Additional Resources

More information, including a Data Supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net. The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline update.

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