General

Guideline Title


Bibliographic Source(s)


Guideline Status

This is the current release of the guideline.


The American Society of Clinical Oncology reaffirmed the currency of this guideline in 2015.

Recommendations

Major Recommendations

Clinical Question 1

Should Hospitalized Patients With Cancer Receive Anticoagulation for Venous Thromboembolism (VTE) Prophylaxis?

Recommendation 1.1. Hospitalized patients who have active malignancy with acute medical illness or reduced mobility should receive pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.

Recommendation 1.2. Hospitalized patients who have active malignancy without additional risk factors may be considered for pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.

Recommendation 1.3. Data are inadequate to support or oppose thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion or in patients undergoing stem-cell/bone marrow transplantation.

Clinical Question 2
Should Ambulatory Patients With Cancer Receive Anticoagulation for VTE Prophylaxis During Systemic Chemotherapy?

Recommendation 2.1. Routine pharmacologic thromboprophylaxis is not recommended in cancer outpatients.

Recommendation 2.2. Based on limited randomized controlled trial (RCT) data, clinicians may consider low–molecular weight heparin (LMWH) prophylaxis on a case-by-case basis in highly selected outpatients with solid tumors receiving chemotherapy. Consideration of such therapy should be accompanied by a discussion with the patient about the uncertainty concerning benefits and harms as well as dose and duration of prophylaxis in this setting.

Recommendation 2.3. Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone should receive pharmacologic thromboprophylaxis with either aspirin or LMWH for lower-risk patients and LMWH for higher risk patients.

Clinical Question 3
Should Patients With Cancer Undergoing Surgery Receive Perioperative VTE Prophylaxis?

Recommendation 3.1. All patients with malignant disease undergoing major surgical intervention should be considered for pharmacologic thromboprophylaxis with either unfractionated heparin (UFH) or LMWH unless contraindicated because of active bleeding or high bleeding risk.

Recommendation 3.2. Prophylaxis should be commenced preoperatively.

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.

Recommendation 3.4. A combined regimen of pharmacologic and mechanical prophylaxis may improve efficacy, especially in the highest-risk patients.

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 should be considered for patients undergoing major abdominal or pelvic surgery for cancer who have high-risk features such as restricted mobility, obesity, history of VTE, or with additional risk factors as listed in Table 3 of the original guideline document. In lower-risk surgical settings, the decision on appropriate duration of thromboprophylaxis should be made on a case-by-case basis considering the individual patient.

Clinical Question 4
What is the Best Method for Treatment of Patients With Cancer with Established VTE to Prevent Recurrence?

Recommendation 4.1. 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).

Recommendation 4.2. For long-term anticoagulation, LMWH for at least 6 months is preferred because of improved efficacy over vitamin K antagonists (VKAs). VKAs are an acceptable alternative for long-term therapy if LMWH is not available.

Recommendation 4.3. Anticoagulation with LMWH or VKAs beyond the initial 6 months may be considered for select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy.

Recommendation 4.4. The insertion of a vena cava filter is only indicated for patients with contraindications to anticoagulant therapy (see Table 4 in the original guideline document). It may be considered as an adjunct to anticoagulation in patients with progression of thrombosis (recurrent VTE or extension of existing thrombus) despite optimal therapy with LMWH.

Recommendation 4.5. For patients with primary central nervous system (CNS) malignancies, anticoagulation is recommended for established VTE as described for other patients with cancer. Careful monitoring is necessary to limit the risk of hemorrhagic complications.

Recommendation 4.6. Use of novel oral anticoagulants for either prevention or treatment of VTE in patients with cancer is not recommended at this time.

Recommendation 4.7. Based on consensus, incidental pulmonary embolus (PE) and deep vein thrombosis (DVT) should be treated in the same manner as symptomatic VTE. Treatment of splanchic or visceral vein thrombi diagnosed incidentally should be considered on a case-by-case basis, considering potential benefits and risks of anticoagulation.

Clinical Question 5
Should Patients With Cancer Receive Anticoagulants in the Absence of Established VTE to Improve Survival?

Recommendation 5.1. Anticoagulants are not recommended to improve survival in patients with cancer without VTE.

Recommendation 5.2. Patients with cancer should be encouraged to participate in clinical trials designed to evaluate anticoagulant therapy as an adjunct to standard anticancer therapies.

Clinical Question 6

What is Known About Risk Prediction and Awareness of VTE Among Patients With Cancer?

Recommendation 6.1. Based on consensus, the Panel recommends that patients with cancer be assessed for VTE risk at the time of chemotherapy initiation and periodically thereafter. Individual risk factors, including biomarkers and cancer site, do not reliably identify patients with cancer at high risk of VTE. In the outpatient setting, risk assessment can be conducted based on a validated risk assessment tool (Table 5 of the original guideline document).

Recommendation 6.2. Based on consensus, the Panel recommends that oncologists educate patients regarding VTE, particularly in settings that increase risk such as major surgery, hospitalization, and while receiving systemic antineoplastic therapy.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Cancer
- Venous thromboembolism (VTE)

Guideline Category

Management
Prevention
Risk Assessment
Treatment

Clinical Specialty

Family Practice
Internal Medicine
Oncology
Surgery

Intended Users

Advanced Practice Nurses
Nurses
Guideline Objective(s)

- To provide recommendations about prophylaxis and treatment of venous thromboembolism (VTE) in patients with cancer in the outpatient, inpatient, and perioperative settings
- To provide recommendations on the use of anticoagulation as a cancer-directed therapy
- To answer the following clinical questions:
  - Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?
  - Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?
  - Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?
  - What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?
  - Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?
  - What is known about risk prediction and awareness of VTE among patients with cancer?

Target Population

Patients with cancer, including:

- Hospitaized patients
- Patients without venous thromboembolism (VTE) receiving chemotherapy on an ambulatory basis
- Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone
- Patients undergoing surgery (perioperative and postoperative periods)
- Patients with recent prior VTE
- Patients without an established VTE

Interventions and Practices Considered

1. Pharmacologic thromboprophylaxis
   - Aspirin
   - Low–molecular weight heparin (LMWH)
   - Unfractionated heparin (UFH)
   - Vitamin K antagonists (VKAs)
2. Preoperative pharmacologic thromboprophylaxis (UFH or LMWH)
3. Combined mechanical plus pharmacologic thromboprophylaxis
4. Insertion of a vena cava filter (with contraindications to anticoagulant therapy)
5. Extended thromboprophylaxis
6. Patient education

Major Outcomes Considered

- Incidence and severity of
  - Symptomatic and asymptomatic venous thromboembolism (VTE)
  - Symptomatic and asymptomatic arterial thromboembolism
  - Bleeding events
  - Pulmonary embolism (PE)
  - Deep vein thrombosis (DVT)
- Mortality
Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

2013 Guideline

Literature Search Strategy

The effectiveness search included the MEDLINE, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials databases. Conference proceedings from annual meetings of the American Society of Clinical Oncology (ASCO), the American Society of Hematology, the European Society of Medical Oncology, and the International Society of Thrombosis and Hemostasis were searched through 2012 or the most recent year available. The risk assessment search was completed in MEDLINE.

Reference lists from seminal articles, guidelines from other organizations, and recent review articles were hand searched for additional citations. The Update Committee reviewed the list of included reports for completeness. Subject headings and keywords used in the efficacy literature search included four major categories: venous thromboembolism (VTE), anticoagulation, malignancy, and randomized controlled trials (RCTs). The full search string is available in the Data Supplement of the original guideline document (see the "Availability of Companion Documents" field).

The risk literature search also included four major categories: risk assessment, VTE, cancer, and cohort studies.

Inclusion and Exclusion Criteria

Articles for the efficacy systematic review were selected for inclusion if they were RCTs or systematic reviews of RCTs that assessed the efficacy and safety of anticoagulation in patients with cancer and included at least 50 patients per arm. Only data from conference proceedings available as full presentations or posters were included. For the risk systematic review, studies from the ambulatory setting that either developed or validated risk models were included. Only reports that included multivariate analyses were eligible. Risk assessment models limited to single cancer types were excluded.

2015 Reaffirmation

Guideline Update Process

PubMed and the Cochrane Library were searched for randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines for the period from November 5, 2012, through July 2014. The disease and intervention search terms were those that were used for the 2013 guideline update. An update committee, formed in accordance with the ASCO Conflict of Interest Management Procedures for Clinical Practice Guidelines, reviewed the abstracts that were identified for predefined signals that would suggest the need to change a previous recommendation. Additional information about the results of the updated literature search and 2014 search strategy string and results are available in the 2014 Data Supplement (see the "Availability of Companion Documents" field). A QUOROM diagram of the updated search and the clinical questions are also provided in the 2014 Data Supplement.

Results

The search yielded 53 publications. After careful review of the identified publications, the update committee concluded that there were no results that would change the 2013 guideline recommendations. A bibliography of the results of the updated literature search is provided in the 2014 Data Supplement.

Number of Source Documents

42 publications met eligibility criteria, including 16 systematic reviews and 24 randomized controlled trials.
Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

Eligible reports for both reviews were preliminarily identified after the literature search. Full-text copies were obtained to further assess eligibility. Articles that met eligibility for the efficacy search underwent data extraction by American Society of Clinical Oncology (ASCO) staff for study design and quality, patient characteristics, outcomes, and adverse events. Outcomes of interest included symptomatic and asymptomatic thrombotic events found on screening, major and minor bleeding, early and overall mortality, sudden death, and adverse events. For the risk review, data extraction included study characteristics, quality, and risk assessment model development and evaluation. Outcomes of interest included factors incorporated into the risk assessment model, model equation, and outcomes according to risk.

Evidence summary tables (Data Supplement of the original guideline document, [see the "Availability of Companion Documents" field]) were reviewed for accuracy and completeness by an ASCO staff member who was not involved in data extraction. Disagreements were resolved through discussion; the Steering Committee was consulted if necessary.

Study Quality

Trial characteristics from the randomized controlled trials (RCTs) were extracted to evaluate the potential for bias. Study quality was also assessed for the reports in the risk systematic review.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The American Society of Clinical Oncology (ASCO) first published an evidence-based clinical practice guideline on prophylaxis and treatment of venous thromboembolism (VTE) in 2007. ASCO guidelines are updated at intervals determined by an Update Committee; this is a full guideline update. Table 1 in the original guideline document provides a summary of the 2007 and 2012 guideline recommendations.

An Update Committee was formed to review data published since the initial guideline and update recommendations, as warranted, considering evidence identified by the systematic review.

The Update Committee met in July 2012 and had a second meeting via teleconference. During those meetings, the Update Committee reviewed evidence identified by the systematic review and revised guideline recommendations. Additional work on the guideline was completed electronically. The steering committee and lead ASCO staff person prepared an updated guideline to share with the Update Committee members for review.

Rating Scheme for the Strength of the Recommendations
Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

As per standard practice, the guideline was submitted to Journal of Clinical Oncology for review. The Venous Thromboembolism (VTE) Update Committee and the ASCO Clinical Practice Guideline Committee reviewed and approved this guideline document before publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

In general, the evidence was limited to randomized controlled trials (RCTs) and systematic reviews (with or without meta-analyses).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate venous thromboembolism prophylaxis and treatment in patients with cancer

Potential Harms

- Hemorrhagic complications of anticoagulation
- Caution and close monitoring are necessary in those with renal impairment, cognitive decline, and without family or nearby support

Contraindications

Contraindications

Contraindications and Other Considerations to Withhold Therapeutic Anticoagulant Therapy in Patients With Cancer and Venous Thromboembolism (VTE)*

Absolute Contraindications†

- Active major, serious, or potentially life-threatening bleeding not reversible with medical or surgical intervention, including but not limited to any active bleeding in a critical site (i.e., intracranial, pericardial, retroperitoneal, intraocular, intra-articular, intraspinal)
- Severe, uncontrolled malignant hypertension
- Severe, uncompensated coagulopathy (e.g., liver failure)
- Severe platelet dysfunction or inherited bleeding disorder
Persistent, severe thrombocytopenia (<20,000/µL)
Surgery or invasive procedure, including but not limited to lumbar puncture, spinal anesthesia, and epidural catheter placement

Relative Contraindications‡:

- Intracranial or spinal lesion at high risk for bleeding
- Active peptic or other gastrointestinal (GI) ulceration at high risk of bleeding
- Active but non-life-threatening bleeding (e.g., trace hematuria)
- Intracranial or central nervous system (CNS) bleeding within past 4 weeks
- Major surgery or serious bleeding within past 2 weeks
- Persistent thrombocytopenia (<50,000/µL)

Patients for Whom Anticoagulation is of Uncertain Benefit

- Patient receiving end-of-life/hospice care
- Very limited life expectancy with no palliative or symptom reduction benefit
- Asymptomatic thrombosis with concomitant high risk of serious bleeding

Patient Characteristics and Values

- Preference or refusal
- Nonadherence to dosing schedule, follow-up or monitoring

*These criteria are specific for therapeutic doses of anticoagulation and should not be applied to prophylactic doses of anticoagulation.
†Absolute contraindications are situations in which anticoagulation should not be administered because the risk of harm associated with bleeding is likely to exceed the potential benefit from anticoagulation.
‡Relative contraindications are situations in which anticoagulation may be administered if the risk of recurrent or progressive thrombosis is estimated to exceed the risk of bleeding.

Qualifying Statements

The practice guideline is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This guideline does not recommend any particular product or course of medical treatment. Use of the practice guideline is voluntary. Additional information is available at the American Society of Clinical Oncology (ASCO) Web site [link]

Study Quality and Limitations of the Literature

Publications identified by the systematic review varied with respect to potential for bias, ranging from low to high. A majority of the trials were of moderate quality. Specific quality issues are discussed within the section for the relevant clinical question.

Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, please see the ASCO Web site [link]

Implementation Tools

Patient Resources
Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need
- Getting Better
- Living with Illness

IOM Domain
- Effectiveness
- Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)


Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2007 Dec (revised 2013 Jun; reaffirmed 2015 Feb)

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

Guideline Committee
American Society of Clinical Oncology (ASCO) Clinical Guideline Update Committee

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Financial Disclosures/Conflicts of Interest

The Update Committee was assembled in accordance with American Society of Clinical Oncology's (ASCO's) Conflict of Interest Management Procedures for Clinical Practice Guidelines ("Procedures," summarized at the ASCO Web site). Members of the Update Committee completed ASCO's disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with the Procedures, the majority of the members of the Update Committee did not disclose any such relationships.

Although all authors completed the disclosure declaration, the following author(s) and/or an author's immediate family member(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors. Authors marked with an asterisk (*) are participants in ASCO's Disclosure Management System Pilot; their disclosure is not limited to subject matter under consideration in this article and includes payments to themselves, an immediate family member (I), and/or their institutions (INST). For information on the pilot program, or to provide feedback, please visit the ASCO Web site.

**Employment or Leadership Position:** None Consultant or Advisory Role: Alok Khorana, Daiichi Sankyo (C), Johnson & Johnson (C), Eisai (C), sanofi-aventis (C), LEO Pharma (C), Bristol-Myers Squibb (C), Genentech (C), Eli Lilly (C); Agnes Lee, Bristol-Myers Squibb (C); Charles W. Francis, Eisai (C); Ajay K. Kakkar, Bayer HealthCare Pharmaceuticals (C), Boehringer Ingelheim (C), Eisai (C), GlaxoSmithKline (C), Pfizer (C), sanofi-aventis (C); Howard A. Liebman, Eisai (C), GlaxoSmithKline (C), Johnson & Johnson (C), sanofi-aventis (C) **Stock Ownership:** None **Honoraria:** Alok Khorana, Eli Lilly, sanofi-aventis, Daiichi Sankyo, Johnson & Johnson, Eisai, LEO Pharma, Bristol-Myers Squibb, Genentech, Agnes Lee, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim, LEO Pharma, Pfizer, sanofi-aventis; Juan Ignacio Arcelus, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb, Pfizer, sanofi-aventis Research Funding: *Gary H. Lyman, Amgen; Alok Khorana, LEO Pharma, sanofi-aventis; Agnes Lee, LEO Pharma; Charles W. Francis, Eisai; Ajay K. Kakkar, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim, Eisai, GlaxoSmithKline, Pfizer, sanofi-aventis Expert Testimony: None Other Remuneration: None

Guideline Status
This is the current release of the guideline.


The American Society of Clinical Oncology reaffirmed the currency of this guideline in 2015.

Guideline Availability

Electronic copies: Available from the Journal of Clinical Oncology Web site.

Print copies: Available from American Society of Clinical Oncology, Cancer Policy and Clinical Affairs, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; E-mail: guidelines@asco.org.

Availability of Companion Documents

The following are available:


Patient Resources

The following is available:


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