

Central Venous Catheter Care for the Patient With Cancer: American Society of Clinical Oncology Clinical Practice Guideline

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Editor's note: This is a summary of the literature that was used to inform the American Society of Clinical Oncology Clinical Practice Guideline for Central Venous Catheter Care for the Patient With Cancer and provides recommendations with brief discussions of the relevant literature for each. Evidence tables with details about the studies and meta-analyses cited are provided in Data Supplements 1 and 2 at www.asco.org/guidelines/cvc.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

Purpose

To develop an evidence-based guideline on central venous catheter (CVC) care for patients with cancer that addresses catheter type, insertion site, and placement as well as prophylaxis and management of both catheter-related infection and thrombosis.

Methods

A systematic search of MEDLINE and the Cochrane Library (1980 to July 2012) identified relevant articles published in English.

Results

The overall quality of the randomized controlled trial evidence was rated as good. There is consistency among meta-analyses and guidelines compiled by other groups as well.

Recommendations

There is insufficient evidence to recommend one CVC type or insertion site; femoral catheterization should be avoided. CVC should be placed by well-trained providers, and the use of a CVC clinical care bundle is recommended. The use of antimicrobial/antiseptic-impregnated and/or heparin-impregnated CVCs is recommended to decrease the risk of catheter-related infections for short-term CVCs, particularly in high-risk groups; more research is needed. The prophylactic use of systemic antibiotics is not recommended before insertion. Data are not sufficient to recommend for or against routine use of antibiotic flush/lock therapy; more research is needed. Before starting antibiotic therapy, cultures should be obtained. Some life-threatening infections require immediate catheter removal, but most can be treated with antimicrobial therapy while the CVC remains in place. Routine flushing with saline is recommended. Prophylactic use of warfarin or low-molecular weight heparin is not recommended, although a tissue plasminogen activator (t-PA) is recommended to restore patency to occluded catheters. CVC removal is recommended when the catheter is no longer needed or if there is a radiologically confirmed thrombosis that worsens despite anticoagulation therapy.

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INTRODUCTION

The management of the patient with cancer demands stable venous access that is used for a wide range of indications including chemotherapy, blood product and antibiotic administration, fluid resuscitation, and access to the bloodstream for clinical monitoring and microbial culturing. The use of long-term central venous catheters (CVCs) can also decrease patient anxiety associated with repeated venipunctures. The number and variety of CVCs used in oncology practices during the past 30 years have greatly increased, but the most commonly used long-term devices include: surgically implanted cuffed tunneled central venous catheters, subcuta-

neous implanted ports, peripherally inserted CVCs (PICCs), and percutaneous noncuffed or tunneled catheters. During the past decade, the composition of these devices has changed, the catheter size and lumen number have increased, and CVCs impregnated with anti-infective material or antibiotics and heparin have become available. A CVC care clinical bundle^{1,2} is now the standard of care. The insertion and care of a CVC require a multidisciplinary approach, involving medical oncologists/hematologists, nurses, interventional radiologists, surgeons, infectious disease specialists, and often a specialized CVC care team.³

CVCs have a considerable potential for serious complications, which are often underappreciated.

Early complications related to CVC placement include bleeding, cardiac arrhythmia, malposition, air embolism, and pneumothorax and, rarely, injury to vessels or nerves. Late complications include infection, thrombosis, and catheter malfunction. Patients with cancer with implantable port systems were found to experience a median of 0.2 infections per 1,000 catheter-days (range, 0 to 2.7 per 1,000 catheter-days)⁴ versus a risk that ranges from 1.4 to 2.2 infections per 1,000 catheter-days for subcutaneous tunneled CVCs.^{5,6} Some infections can be life threatening and require immediate catheter removal, whereas others can be treated while the catheter remains in place. The incidence of CVC-associated thrombi in patients with cancer varies in different series, from 27% to 66%, when routine screening with venography is performed. Most patients with CVC thrombi are asymptomatic.⁷ Reported rates of symptomatic thrombi also vary widely, from 0.3% to 28%.⁷⁻¹⁰ Infection or thrombosis of a CVC can

be an indication for removal, which can result in prolonged and costly hospitalizations and significant delays in treatment. The purpose of this guideline is to assist in care and decision making for patients with cancer who often have long-term CVCs and to identify areas of controversy, promoting future research and clinical trials. This is a new American Society of Clinical Oncology (ASCO) guideline focused on CVC care for patients with cancer.

GUIDELINE QUESTIONS

Clinical Question 1

In patients with cancer, does catheter type, insertion site, or placement technique affect complication rates?

THE BOTTOM LINE

American Society of Clinical Oncology Clinical Practice Guideline for Central Venous Catheter Care for the Patient With Cancer

Intervention

- Placement of a central venous catheter (CVC) in adult and pediatric patients with cancer and the subsequent prevention and management of catheter-related infections and thromboses

Target Audience

- Medical oncologists/hematologists, nurses, interventional radiologists, surgeons, infectious disease specialists, and specialized CVC care teams

Key Recommendations

- There is insufficient evidence to recommend a specific type of CVC or insertion site, but femoral vein insertion should be avoided, except in certain emergency situations
- CVCs should be placed by well-trained health care providers
- Use of a CVC clinical care bundle is recommended
- Use of antimicrobial/antiseptic-coated CVCs and/or heparin-impregnated CVCs has been shown to be beneficial, but the benefits and costs must be carefully considered before they can be routinely used
- Prophylactic use of systemic antibiotics is not recommended before CVC insertion
- Cultures of blood from the CVC and/or tissue at the entrance-exit sites should be obtained before initiation of antibiotic therapy; most clinically apparent exit- or entrance-site infections as well as bloodstream infections can be managed with appropriate microbial therapy, so CVC removal may not be necessary; antimicrobial agents should be optimized once the pathogens are identified; catheter removal should be considered if the infection is caused by an apparent tunnel or port-site infection, fungi, or nontuberculous mycobacteria or if there is persistent bacteremia after 48 to 72 hours of appropriate antimicrobial treatment
- Routine flushing with saline is recommended
- Prophylactic warfarin and low-molecular weight heparin have not been shown to decrease CVC-related thrombosis, so routine use is not recommended
- Tissue plasminogen activator (t-PA) is recommended to restore patency in a nonfunctioning CVC; CVC removal is recommended when the catheter is no longer needed, if there is a radiologically confirmed thrombosis that does not respond to anticoagulation therapy, or if fibrinolytic or anticoagulation therapy is contraindicated

Methods

- Systematic review and analysis of the medical literature on CVC care for patients with cancer by ASCO CVC Care Expert Panel

Additional Information

- Data Supplements, including evidence tables, and clinical tools and resources can be found at <http://www.asco.org/guidelines/cvc>

Clinical Question 2

What is effective prophylaxis for the prevention of catheter-related infections?

Clinical Question 3

What are effective treatments for the management of catheter-related infections?

Clinical Question 4

What is effective prophylaxis for the prevention of catheter-related thrombosis?

Clinical Question 5

What are effective treatments for the management of catheter-related occlusions?

CLINICAL PRACTICE GUIDELINES

Practice guidelines are systematically developed statements that assist practitioners and patients in making decisions about care. Attributes of good guidelines include validity, reliability, reproducibility, clinical applicability, flexibility, clarity, multidisciplinary process, review of evidence, and documentation. Guidelines may be useful in producing better care and decreasing cost. Specifically, use of clinical guidelines may provide:

1. Improvements in outcomes
2. Improvements in medical practice
3. A means for minimizing inappropriate practice variation
4. Decision support tools for practitioners
5. Points of reference for medical orientation and education
6. Criteria for self-evaluation
7. Indicators and criteria for external quality review
8. Assistance with reimbursement and coverage decisions
9. Criteria for use in credentialing decisions
10. Identification of areas where future research is needed

METHODS

Panel Composition

The ASCO Clinical Practice Guidelines Committee convened an Expert Panel consisting of experts in clinical medicine and research relevant to CVC care in patients with cancer, including medical and surgical oncologists and oncology nurses. Academic and community practitioners and a patient representative were also part of the Panel. The Panel members are listed in Appendix Table A1 (online only).

Literature Review and Analysis

Literature search strategy. MEDLINE (Pubmed) and the Cochrane Collaboration Library were searched with the date parameters of January 1980 through January 2012. Reference lists of related reports and review articles were scanned for additional citations. Details about the literature search and results are provided in Data Supplements 3 and 4 at www.asco.org/guidelines/cvc.

Inclusion and exclusion criteria. The systematic review conducted for this guideline included 108 randomized controlled trials (RCTs) in which adult or pediatric patients with cancer were randomly assigned to an appropriate control group or to an intervention of interest, including CVC type, placement site, or strategies to prevent or manage infection or thrombosis. Studies were included only if they had catheter type, placement site, infection, or thrombosis as a priori planned primary or secondary outcome and described a method of regular patient follow-up to ensure a consistent and identical identification of the outcomes in both study arms. Infection and/or

thrombosis had to be confirmed either through objective tests (blood or imaging) and/or clinical observation. Results of meta-analyses are also reported in the Literature Review and Analysis sections pertaining to each recommendation; other guidelines, particularly those by the Centers for Disease Control and Prevention (CDC), originally published by the CDC in August 2002 and updated in 2011, and the Infectious Disease Society of America (IDSA), informed the decisions of the Panel.

Trials were excluded if they were nonrandomized reports or posthoc subgroup analyses or if only a minority of the patients studied had cancer. RCTs were also excluded if patients with CVCs were compared with patients with peripheral catheters.

Data extraction. Two reviewers independently extracted the data on basic study design, patient characteristics, interventions, study outcomes, follow-up, and measures of study quality. Any discrepancies between reviewers were resolved by consensus.

Study quality. Overall study quality was evaluated by the Jadad method. The evidence tables in Data Supplements 1 and 2 at www.asco.org/guidelines/cvc include information on randomization, blinding, allocation concealment, withdrawals, and intention-to-treat analyses. Meta-analyses were evaluated using the Oxman-Guyatt Index, in which questions must be clearly specified, target populations identified and accessed, and appropriate information obtained in an unbiased fashion.

Evidence-Based Guideline Development Process

The entire Panel met one time in person and a writing group met subsequently; additional work on the guideline was completed through a steering group and e-mail. The Panel and writing group drafted guideline recommendations and distributed writing assignments. All members of the Panel participated in the preparation of the draft guideline document, which was then disseminated for review and approval by the entire Panel. The guideline was submitted to *Journal of Clinical Oncology* for peer review. Feedback from additional external reviewers was also solicited. The content of the guideline and the manuscript was reviewed and approved by the ASCO Clinical Practice Guideline Committee before publication.

Guideline Policy

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. The guideline, evidence tables, and data supplements are available at <http://www.asco.org/guidelines/cvc>.

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the ASCO Conflicts of Interest Management Procedures for Clinical Practice Guidelines (summarized at www.asco.org/guidelines/coi).

Revision Dates

At annual intervals, the Panel co-chairs will determine the need for revisions to the guideline based on an examination of current literature. If necessary, the entire Panel or an update committee will be reconvened to discuss potential changes. When appropriate, the Panel will recommend revised recommendations to the Clinical Practice Guideline Committee for approval.

RESULTS

Literature Review Results and Limitations of the Literature

A total of 108 RCTs with results specific to patients with cancer (Data Supplement 1 at www.asco.org/guidelines/cvc), 25 meta-analyses or systematic reviews (Data Supplement 2 at www.asco.org/guidelines/cvc), and several existing guidelines¹¹⁻¹⁶ were identified in the search of the literature. RCTs were considered eligible for data extraction if the majority of patients had cancer. It should be noted that many of the

trials had small numbers of patients, and there was considerable heterogeneity in trial design, types of catheters used, placement techniques, and methods of evaluating end points, even among trials addressing the same question. In addition, clinical practices have changed over the years, and the Panel focused on more-recent trials whenever possible. Nonetheless, the overall quality of the evidence was rated as good, as evidenced in part by the consistency among meta-analyses and guidelines compiled by other groups.

GUIDELINE RECOMMENDATIONS

On the basis of the evidence and the expert opinion of the CVC Care Panel, the following recommendations are offered in Table 1.

Catheter Type, Insertion Site, and Placement

A CVC can be designated by its pathway to the vessel (eg, tunneled v nontunneled or implanted); its site of insertion (eg, subclavian, femoral, internal jugular, or PICC); or its composition, length, or special characteristic (eg, presence or absence of a cuff; impregnation with heparin, antibiotics, or antiseptics; single or multiple lumens). When selecting the proper CVC, factors to consider are the purpose, the expected duration of the catheter, who will maintain the device, and patient preference. The use of a CVC should be considered for patients with cancer (adults and children) with limited peripheral venous access, for those receiving regimens that require prolonged or continuous intravenous (IV) infusions of multiple chemotherapeutic or supportive care agents, for those requiring repeated blood sampling or clinical monitoring, and for those expected to receive a vesicant as

Table 1. ASCO Recommendations for CVC Care

Clinical Question	Recommendation
1. In patients with cancer, does catheter type, insertion site, or placement affect complication rates?	<p>1.1. There is insufficient evidence to recommend one type of CVC routinely for all patients with cancer; the choice of catheter should be influenced by the expected duration of use, chemotherapy regimens, and patient ability to provide care; the minimum number of lumens essential for the management of the patient is recommended; these issues should be discussed with the patient</p> <p>1.2. There is insufficient evidence to recommend one insertion site or approach (left sided or right sided) for tunneled CVCs for patients with cancer; individual risks and benefits (comfort, security, maintenance of asepsis) of the catheter site should be considered; the Panel recommends that CVC insertion into the femoral vein be avoided because of increased infection risks and concerns about thrombosis, except in certain emergency situations</p> <p>1.3. Most CVC placement in patients with cancer is performed as an elective procedure; although image-guided insertion (eg, ultrasound guided, fluoroscopy) of CVCs is recommended, well-trained providers who use the landmark method regularly (eg, for subclavian or internal jugular) may have high rate of success and low incidence of acute and/or chronic complications</p>
2. What is effective prophylaxis for the prevention of catheter-related infections?	<p>2.1. CVC care clinical bundle (including hand hygiene, maximal barrier precautions, chlorhexidine skin antiseptics during catheter insertion, optimal catheter site selection, and assessment of CVC necessity) is recommended for placement and maintenance of all CVCs to prevent infections; there is no evidence that particular dressing types or more frequent IV set and/or dressing changes decrease risk of infection; use of topical antibiotic ointment or cream on insertion sites is not recommended because of potential to promote fungal infections and resistance to antimicrobials; scheduled guidewire exchange of CVC may be associated with greater risk of infection versus catheter replacement at new vascular site; thus, guidewire exchange is not routinely recommended, unless access options are limited</p> <p>2.2. Use of antimicrobial/antiseptic-impregnated or -coated CVCs (CH-SS or minocycline/rifampin) and/or heparin-impregnated catheters is recommended to decrease risk of catheter-related infections for short-term CVCs, particularly in high-risk groups such as bone marrow transplantation recipients or patients with leukemia; however, relative benefit and increased cost must be carefully considered before they are routinely used</p> <p>2.3. Prophylactic use of systemic antibiotics (IV or oral) before insertion of long-term CVCs is not recommended</p> <p>2.4. There are conflicting data about the relative value of prophylactic heparin with saline flushes to prevent catheter-associated bloodstream infections or thrombosis; data are not sufficient to recommend for or against routine use of antibiotic-flush/antibiotic-lock therapy</p>
3. What are effective treatments for the management of catheter-related infections?	<p>3.1. Cultures of blood from the catheter and when appropriate of soft tissues at entrance-exit sites or tunnel should be obtained before initiation of antibiotic therapy; most exit- or entrance-site infections can be treated successfully with appropriate antimicrobial therapy without the need for catheter removal, although removal is usually needed for clinically apparent tunnel or port-site infections; antimicrobial agents should be optimized once pathogens are identified and antibiotic susceptibilities defined</p>
4. What is effective prophylaxis for the prevention of catheter-related thrombosis?	<p>4.1. Use of systemic anticoagulation (warfarin, LMWH, UFH) has not been shown to decrease incidence of catheter-associated thrombosis; therefore, routine prophylaxis with anticoagulants is not recommended for patients with cancer with CVCs; routine flushing with saline of the CVC to prevent fibrin buildup is recommended</p> <p>4.2. Data are insufficient to recommend routine use of urokinase (not available in the United States) and/or other thrombolytics to prevent catheter occlusion</p>
5. What are effective treatments for the management of occluded catheters?	<p>5.1. Instillation of 2-mg t-PA is recommended to restore patency and preserve catheter function</p> <p>5.2. Although it is appropriate to try to clear thrombosis with the CVC in place, if there is radiologically confirmed thrombosis that does not respond to fibrinolytic therapy or if fibrinolytic or anticoagulation therapy is contraindicated, catheter removal is recommended; prolonged retention of unneeded CVCs can lead to significant problems associated with thrombosis and fibrosis; 3 to 6 months of anticoagulant therapy with LMWH or LMWH followed by warfarin (INR, 2.0 to 3.0) is recommended for treatment of symptomatic CVC thrombosis, with duration depending on clinical issues in individual patients</p>

Abbreviations: ASCO, American Society of Clinical Oncology; CH-SS, chlorhexidine and silver sulfadiazine; CVC, central venous catheter; INR, international normalized ratio; IV, intravenous; LMWH, low-molecular weight heparin; t-PA, tissue plasminogen activator; UFH, unfractionated heparin.

part of their treatment regimen. It should be noted, however, that many regimens containing vesicants can be administered safely to patients with good peripheral venous access by skilled infusion nurses. Patient education about types of CVCs facilitates an informed decision before catheter placement, because the decision about the type of catheter should involve both the health care provider and the patient (see Patient and Clinician Communication section). A table of CVC types and risks of infection is provided in Data Supplement 5 at www.asco.org/guidelines/cvc.

Clinical Question 1

In patients with cancer, does catheter type, insertion site, or placement affect complication rates?

Recommendation 1.1. There is insufficient evidence to recommend one type of CVC routinely for all patients with cancer. The choice of catheter should be influenced by the expected duration of use, the chemotherapy regimen, and the patient's ability to provide care. The minimum number of lumens essential for the management of the patient is recommended. These issues should be discussed with the patient.

Literature review and analysis. Ten RCTs¹⁷⁻²⁶ and three meta-analyses^{6,27,28} addressed these issues. They supported the conclusions that single- or double-lumen (*v* triple) CVCs should be used whenever feasible; and that, for a patient who requires more intensive therapy (ie, hematopoietic cell transplantation recipient, patient with acute leukemia), a subcutaneous port is often not adequate to meet all the patient's clinical needs. In one meta-analysis,⁶ the authors reviewed 200 prospective studies in adult patients. Catheter types were compared using the mean rates of intravascular device (IVD) –related bloodstream infections (BSIs) per 100 IVDs (%) and per 1,000 IVD-days. Point incidence rates of IVD-associated BSIs were lowest for peripheral IV catheters (0.5 per 1,000 IVD-days) and were much higher for short-term, noncuffed, and non-antimicrobial-impregnated CVCs (2.7 per 1,000 IVD-days). Surgically implanted long-term cuffed and tunneled central venous devices resulted in an intermediate infection risk (1.6 per 1,000 IVD-days). PICCs for patients who were hospitalized seemed to pose a substantial risk of infection (2.4%; 2.1 per 1,000 IVD-days), but when assessed just for patients who received both inpatient and outpatient care, the risk of infection was much lower (1.1 per 1,000 IVD-days). The published data do not provide a specific recommendation that could apply to all patients with cancer because of the heterogeneity of the patient populations, variability of the severity of patient illness, different protocols for insertion and site care, and multiple different devices that were tested. Thus, it is critical to carefully consider the patient's present and future needs in making the decision about catheter type.

Recommendation 1.2. There is insufficient evidence to recommend one insertion site or approach (left sided or right sided) for tunneled CVCs for patients with cancer. Individual risks and benefits (comfort, security, and maintenance of asepsis) of the catheter site should be considered. The Panel recommends that CVC insertion into the femoral vein be avoided because of increased infection risks and concerns about thrombosis, except in certain emergency situations.

Literature review and analysis. Evidence from six RCTs^{21,29-33} and one meta-analysis³⁴ indicated that there was no compelling evidence for one insertion site or approach (left sided or right sided). No differences were found for early complication rate among three groups (internal jugular, 0%; 95% CI, 0.0% to 2.7%; subclavian, 0%;

95% CI, 0.0% to 2.7%; cephalic, 1.5%; 95% CI, 0.1% to 5.3%).²⁹ Four of the RCTs^{21,31-33} evaluated subcutaneous tunneled CVCs for patients with malignancies, and taken together, the results of the studies show that subcutaneous tunneling decreases the rate of short- and long-term complications. The CDC guideline¹⁴ and one RCT³⁵ present data that femoral vein CVCs have relatively high bacterial colonization rates when used in adults and an equivalent infection rate in children, and another meta-analysis provides data that a femoral placement can increase thrombosis³⁶; thus, femoral vein insertion should be avoided when other sites are available.

Recommendation 1.3. Most CVC placement in patients with cancer is performed as an elective procedure. Although image-guided insertion (eg, ultrasound guided, fluoroscopy) of CVCs is recommended, well-trained providers who use the landmark method regularly (eg, for subclavian or internal jugular) may have a high rate of success and a low incidence of acute and/or chronic complications.

Literature review and analysis. Four RCTs³⁷⁻⁴⁰ and three meta-analyses⁴¹⁻⁴³ specifically addressed the effectiveness of teams who used image-guided versus landmark-guided CVC placement (eg, subclavian or internal jugular). Using two-dimensional or Doppler ultrasound may achieve lower complication rates.³⁷ In one RCT, although there were no significant differences, in secondary measures (such as pneumothorax, arterial puncture, hematoma), there was 14% misplacement in the blind arm versus only 1% misplacement in the image-guided arm ($P = .001$). However, another RCT³⁸ found that real-time Doppler guidance of subclavian vein catheterization is highly operator dependent and did not increase the success rate or decrease the complication rate of subclavian vein catheterization when compared with the standard technique in high-risk patients, nor was it more useful than the standard technique as a salvage technique after a previous failure of catheterization. Another small RCT³⁹ found that ultrasound techniques did not influence the rate of complication or failure of subclavian vein catheterizations. The authors reported a 12% failure rate ($n = 51$) in the ultrasound group and 12% failure rate ($n = 49$) in the control group. A final RCT⁴⁰ concluded that the surface landmark technique was not as reliable as IV electrocardiography-guided catheter tip placement (satisfactory placement for 16 of 30 patients *v* 30 of 30 patients, respectively).

In meta-analyses,⁴¹⁻⁴³ it was concluded that two-dimensional ultrasound is significantly better than the landmark method. Not all the patients in these meta-analyses had cancer, and thus, there was significant heterogeneity of study results. However, in another meta-analysis,⁴¹ a subgroup analysis suggested improved outcomes for patients with cancer with image-guided CVC insertion.

Infection

The CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections¹⁴ and the IDSA 2009 Update of the Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection⁴⁴ conclude that experienced, educated health care workers or dedicated CVC teams are critical for infection prophylaxis for CVCs in patients with cancer. The CDC and IDSA guidelines were written for all patients but provide specific recommendations regarding diagnosis and management of infection for patients with cancer as well. Two RCTs focusing on patients with cancers^{45,46} reported that catheter-related infections are largely preventable and that education for all providers and systematic individualized, supervised patient and caregiver education are effective and affordable and decrease infection rates.

Catheter-related infections can be grouped into one of three categories: one, localized entrance- or exit-site infections; two, tunnel and/or port-pocket infections; and three, catheter-associated BSIs (catheter-related BSIs). The pathogens that cause catheter-associated infections have changed during the past decades, influenced by changing catheter materials, antimicrobial impregnation of the catheters, sites of catheter placement, and the antimicrobial selection that occurs as a result of changing antibiotic prescribing habits. More detailed information is available at Definitions of Infections Associated With CVCs and Treatment, provided in Data Supplement 6 at www.asco.org/guidelines/cvc. In general, entrance- or exit-site infections are associated with a low incidence of BSIs. However, tunnel or port-site catheter BSIs are not uncommon and can be a significant cause of morbidity. The consequences of catheter-related infections depend on several factors such as the type of CVC, the catheter placement location, and the patient's performance status, including associated myelo/immunosuppression. Patients with cancer with implantable port systems were found to experience a median of 0.2 infections per 1,000 catheter-days (range, 0 to 2.7 per 1,000 catheter-days)⁴ versus a risk that ranges from 1.4 to 2.2 infections per 1,000 catheter-days for subcutaneous tunneled CVCs.^{5,6} However, this difference may be artifactual, because patients who receive implantable subcutaneous ports usually receive much less intensive cancer therapy. The duration of antimicrobial therapy for the treatment of catheter-associated infections ranges from 7 to 21 days, and success rates have ranged from 60% to 91%.⁴⁷ It is important to note that both duration of treatment and treatment success are highly dependent on the organism(s) responsible for the infection, the need for catheter or subcutaneous port removal, and the patient's underlying neutrophil count. Early catheter removal is critical for some infections, whereas premature or unnecessary catheter removal may interrupt treatment and increase patient discomfort, anxiety, and cost because of the need for placement of another catheter.

Clinical Question 2

What is effective prophylaxis for the prevention of catheter-related infections?

Recommendation 2.1. A CVC care clinical bundle (including hand hygiene, maximal barrier precautions, chlorhexidine skin antiseptics during catheter insertion, optimal catheter site selection, and assessment of CVC necessity) is recommended for the placement and maintenance of all CVCs to prevent infections (Table 2). There is no evidence that particular dressing types or more frequent IV set and/or

dressing changes decrease the risk of infection. The use of topical antibiotic ointment or cream on insertion sites is not recommended because of the potential to promote fungal infections and resistance to antimicrobials. A scheduled guidewire exchange of CVCs may be associated with a greater risk of infection compared with catheter replacement at a new vascular site, and thus, guidewire exchange is not routinely recommended unless access options are limited.

Literature review and analysis. CVC clinical care bundles have been validated as a highly effective approach to decrease catheter-related BSIs.^{1,2,16,48,49} As has been shown in many RCTs, including three performed in patients with cancer, and in meta-analyses, antiseptic chlorhexidine-based preparations used at the time of insertion decrease the incidence of CVC-related infections by 40% to 50% compared with povidone-iodine solutions.⁵⁰⁻⁵³ Of note, one meta-analysis conducted in 2006⁵³ also assessed the effect of an antiseptic chlorhexidine-impregnated dressing on the risk of vascular and epidural catheter bacterial colonization and infection. The chlorhexidine-impregnated dressing substantially reduced the risk of intravascular catheter or exit-site bacterial colonization (14.8% v 26.9%; odds ratio [OR], 0.47; $P < .001$). In contrast, in eight RCTs,⁵⁴⁻⁶¹ patients with entrance- or exit-site dressings, combined with antibiotic ointments applied at the insertion site, experienced a higher incidence of catheter-related infections than those patients for whom no antibiotic ointment or cream was used.

Several RCTs, systematic reviews, and meta-analyses conducted among patients with cancer have addressed the frequency of catheter dressing changes, replacement of administration sets, and replacement of catheters using a vascular guidewire.^{14,61-65} Scheduled guidewire exchanges of CVCs failed to reduce infection rates compared with replacement at a new site, and indeed, the routine replacement of catheters that are functioning well and do not seem to be infected is not recommended.⁶⁴

Recommendation 2.2. The use of antimicrobial/antiseptic-impregnated or -coated CVCs (chlorhexidine and silver sulfadiazine [CH-SS] or minocycline/rifampin) and/or heparin-impregnated catheters is recommended to decrease the risk of catheter-related infections for short-term CVCs, particularly in high-risk groups such as bone marrow transplantation recipients or patients with leukemia. However, the relative benefit and increased cost must be carefully considered before they are routinely used.

Literature review and analysis. Regarding CVCs impregnated with CH-SS, although the data are mixed, evidence from five RCTs⁶⁶⁻⁷⁰ and two meta-analyses^{71,72} indicates that antimicrobial/

Table 2. CVC Clinical Care Management Bundle

Component	Criteria
Hand hygiene	Every person entering the room during the insertion procedure should perform hand hygiene
Maximal barrier precautions upon insertion	Sterile drape extends from head to toe; all health care providers participating in the procedure employ mask, cap, sterile gown, and sterile gloves
Chlorhexidine skin antiseptics	Skin at the insertion site should be scrubbed with 2% chlorhexidine for 30 seconds and allowed to dry for at least 30 seconds
Optimal catheter site selection	Subclavian vein is the preferred site for nontunneled catheters; avoid femoral site if possible
Assessment of CVC necessity	Prompt removal of CVC line after completion of therapy unless clinical circumstances suggest that further infusional therapy is likely to be necessary in the future

NOTE. Content adapted.^{1,14,48}
Abbreviation: CVC, central venous catheter.

antiseptic-impregnated catheters and cuffs that are coated externally with CH-SS reduce catheter-related BSIs and catheter-related colonization, although there is some evidence to the contrary; one meta-analysis⁷² included studies with methodologic flaws, whereas the nonsignificant findings in three RCTs may have resulted from the development of newer generations of coated catheters.

Regarding CVCs impregnated with minocycline/rifampin, in one large RCT,⁷³ patients with cancer randomly assigned to long-term, nontunneled silicone CVCs impregnated with minocycline and rifampin had lower rates of catheter-related BSIs versus those randomly assigned to nonimpregnated catheters (0.25 v 1.28 infections per 1,000 catheter-days, respectively; $P = .003$). In another RCT,⁷⁴ BSIs were four times less likely to originate from impregnated silicone catheters. In a meta-analysis⁷⁵ of trials not restricted to patients with cancer, rifampicin/minocycline-impregnated CVCs were associated with fewer catheter-related BSIs compared with catheters not impregnated with rifampicin/minocycline.

With regard to CVCs impregnated with heparin, intraluminal fibrin deposition may contribute to the development of infection, and hence, a CVC-impregnated with heparin has the potential to reduce catheter-related infections.⁷⁶ In one RCT of patients with cancer, catheter-related BSIs occurred in 2.5% of patients (three of 120 catheters) with heparin-coated catheters with saline infusion (0.9 events per 1,000 days) versus 9.1% of patients (11 of 120 catheters) with noncoated catheters flushed with unfractionated heparin in the control group (3.5 events per 1,000 days; $P = .027$).⁷⁶

The use of antimicrobial-impregnated CVCs remains somewhat controversial because of cost. Catheters impregnated with CH-SS or minocycline/rifampin (and heparin) are more expensive than standard catheters, although it has been suggested that such catheters could be cost effective in higher-risk patients. It should be noted that a majority of these studies were conducted in patients with short-term CVCs.

Recommendation 2.3. The prophylactic use of systemic antibiotics (IV or oral) before insertion of a long-term CVC is not recommended.

Literature review and analysis. The routine use of systemic antibiotics (IV or oral) before the insertion of a CVC to prevent infection is not recommended.⁴⁴ This recommendation is supported specifically for patients with cancer in one RCT⁷⁷ when the CVC care bundle was used and in four RCTs⁷⁸⁻⁸¹ where prophylactic systemic antibiotics, including vancomycin, did not significantly reduce catheter-related sepsis in patients with cancer. Two small RCTs,^{82,83} with methodologic issues, were inconclusive.

In a Cochrane review of nine RCTs,⁸⁴ CVC tunnel infections were not reduced by the use of prophylactic IV antibiotics before catheter insertion (OR, 0.42; 95% CI, 0.13 to 1.31), although flushing the CVC lumens with antibiotics and heparin seemed to decrease the incidence of Gram-positive infections (OR, 0.43; 95% CI, 0.21 to 0.87). This seemingly positive meta-analysis should be considered carefully before it is translated to most patients with cancer because of the small number of studies and patients.

Recommendation 2.4. There are conflicting data about the relative value of prophylactic heparin with saline flushes to prevent catheter-associated BSIs or thrombosis. Data are not sufficient to recommend for or against the routine use of antibiotic-flush/antibiotic-lock therapy.

Literature review and analysis. Numerous flushing protocols exist, often determined by the manufacturer, which use different volumes and concentrations of heparin, saline, or tissue plasminogen activator (t-PA; or other similar agents) and different frequencies for catheter flushing. Antimicrobial/antiseptic-coated CVCs or heparin-impregnated CVCs are recommended, but conflicting data from one RCT and a meta-analysis^{85,86} suggest that the evidence supporting the use of prophylactic heparin with saline flushes is inconclusive, and definitive randomized comparisons have not been performed. A randomized trial⁸⁷ in the intensive care unit setting evaluating short-term catheter placement did not show a difference between heparin or saline flushes in the rate of catheter thrombosis or catheter-related BSIs. There is a theoretic concern about the clinical syndrome of heparin-associated thrombocytopenia with heparin flushes, although the incidence of this complication has not been determined and seems to be low. The issue of antibiotic flushing and/or antibiotic lock techniques continues to be controversial. The CDC guideline¹⁴ is in favor of these techniques only if the patient is at risk because of a history of previous infections. This is supported by seven RCTs, which reported a significant decrease in catheter-related BSIs or an increase in the time to first episode of catheter-related BSI when antibiotic flush or bacteriostatic saline flushes were used.^{85,88-93} In addition, two other older small RCTs^{94,95} concluded that vancomycin locks or catheter flushes may prevent bacteremia by vancomycin-susceptible organisms in non-neutropenic pediatric patients. This practice must be weighed against the risk that routine use of vancomycin may result in the selection of resistant bacteria. Alternately, two other RCTs^{78,96} reported that the addition of vancomycin to heparin CVC flush solution did not reduce bacteremia with vancomycin-susceptible organisms.

Another meta-analysis⁵ of seven prospective, randomized trials ($n = 463$) compared a vancomycin-heparin lock or flush solution with heparin alone for prevention of BSI. Five of these seven studies were conducted among patients with cancer. The summary risk ratio supporting the use of vancomycin-heparin lock solutions for the prevention of IVD-associated BSIs was 0.49 (95% CI, 0.26 to 0.95; $P = .03$). When vancomycin was instilled in the catheter for a defined period, rather than simply flushing it directly through the catheter, the benefit was greater, with a risk ratio of 0.34 (95% CI, 0.12 to 0.98; $P = .04$). The results of the test for heterogeneity were statistically significant, although heterogeneity was no longer present when one of the studies was removed. Thus, clinicians must be cautious in the interpretation of these data.

Two RCTs addressed the use of urokinase flushes/locks or urokinase-heparin flushes/locks in patients with cancer.^{97,98} Because urokinase is no longer available in the United States, this intervention is no longer applicable in the United States.

Management of Clinically Established Catheter-Related Infection

Determining the source of BSI is often challenging in patients with long-term indwelling CVCs. A helpful diagnostic tool for attempting to diagnose a catheter-related BSI is the differential time to positivity of blood cultures drawn simultaneously through the catheter and a peripheral vein. A blood culture drawn from the CVC that becomes positive at least 120 minutes earlier than simultaneously drawn peripheral vein blood indicates that the catheter is the likely source of infection.⁹⁹ Many approaches to quantify the number of organisms cultured from each site have been proposed. Although not

specific to patients with cancer, there are recommendations for culturing and treatment in the IDSA 2009 Update of the Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection⁴⁴ (pocket card can be found at http://www.idsociety.org/IDSA_Practice_Guidelines/including). The use of antimicrobial agents in patients with cancer and/or neutropenia are also clearly addressed in the IDSA 2010 Update of the Clinical Practice Guideline for the use of Antimicrobial Agents in Neutropenic Patients with Cancer.¹⁰⁰ Information on the management of febrile neutropenia in the outpatient setting can be found at www.asco.org/guidelines/outpatientfn.

Specific therapy with standard antimicrobial agents should be initiated as soon as possible. Catheter-related BSIs are most commonly caused by coagulase-negative staphylococci, *Staphylococcus aureus*, and *Candida* species and less commonly with *Bacillus* species, *Corynebacterium jeikeium*, enterococci (including vancomycin resistant), rapidly growing mycobacteria, and nonlactose fermenting Gram-negative bacilli.⁴⁴ Many of these pathogens are organisms that frequently colonize the skin.

Most BSIs that occur in patients with cancer can be treated effectively without catheter removal. Clinical experience suggests that most bloodstream infections that occur among patients with cancer may not actually originate from or involve the catheter. That said, fungemias or bacteremias with *Bacillus* species, *C jeikeium*, *S aureus*, *P aeruginosa*, or *Stenotrophomonas maltophilia* and nontuberculous mycobacteria (eg, *Mycobacterium chelonae*, *M fortuitum*, *M mucogenicum*, *M abscessus*) often persist despite appropriate antibiotics and then require catheter removal. Catheter removal should also be considered when blood cultures remain positive after 48 hours of antibiotic treatment if no other site of infection has been identified or if bacteremia recurs shortly after completion of a course of antibiotics.

In some patients, catheter removal is not advisable because of platelet transfusion refractory thrombocytopenia and hemorrhagic hazards associated with reimplantation or the absence of other vascular access sites. In these complex cases where the catheter is to be retained, the clinician may find it prudent to prolong the duration of IV antimicrobial therapy.

Clinical Question 3

What are effective treatments for the management of catheter-related infections?

Recommendation 3.1. Cultures of blood from the catheter and when appropriate of soft tissues at the entrance-exit sites or tunnel should be obtained before the initiation of antibiotic therapy. Most exit- or entrance-site infections can be treated successfully with appropriate antimicrobial therapy without the need for catheter removal, although removal is usually needed for clinically apparent tunnel or port-site infections. Antimicrobial agents should be optimized once the pathogens are identified and antibiotic susceptibilities defined.

Immediate catheter removal is recommended for BSIs caused by fungi and nontuberculous mycobacteria (eg, *M chelonae*, *M fortuitum*, *M mucogenicum*, *M abscessus*). BSIs caused by *Bacillus* species, *C jeikeium*, *S aureus*, *P aeruginosa*, *S maltophilis*, and vancomycin-resistant enterococci may be difficult to eradicate with antimicrobial therapy alone, and early catheter removal should be considered. Catheter removal is also recommended for patients with an apparent tunnel or port-site infection, persistent bacteremia after 48 to 72 hours of appropriate antimicrobial treatment in the absence of other obvious

sites or sources of infection, infective endocarditis or peripheral embolization, presence of local catheter-associated complications not responsive to treatment, or relapse of infection with the same pathogen after the completion of an appropriate course of antibiotics.

Literature review and analysis. There are five RCTs^{95,101-104} specifically focused on treatment options for patients with cancer with catheter-related infections. Once the diagnosis of a catheter-related BSI is established or suspected (more information about culturing is available in Data Supplement 7 at www.asco.org/guidelines/cvc), decisions about the duration and type of antimicrobial therapy and catheter removal should be made depending on the patient's disease status, presence of myelosuppression, previous antibiotic exposure, the isolated pathogen, and the type of catheter. In hemodynamically stable patients, depending on the pathogen and in the absence of signs of metastatic infection and/or tunnel or port-site infection, many catheter-related BSIs can be effectively treated without catheter removal, assuming the patient clinically improves, and blood cultures become negative within 48 to 72 hours after antibiotic initiation. Most catheter-related BSIs caused by coagulase-negative *Staphylococcus* can be successfully managed with the catheter in place. These recommendations are consistent with guidelines from other groups, including the IDSA. In contrast, tunnel and port-pocket infections generally require prompt catheter removal coupled with modification of empiric antibiotics based on cultures and the antibiotic susceptibilities of the recovered pathogens.

The duration of systemic antimicrobial therapy after a catheter-related BSI is documented depends on several factors including: catheter removal or retention, response to antimicrobial therapy within the first 48 to 72 hours (resolution of fever and bacteremia), and the development of other complications (embolic tissue infection, septic thrombosis, or endocarditis). In general, for organisms other than coagulase-negative *Staphylococci*, a 14-day course of systemic antimicrobial therapy is adequate, assuming a response to antimicrobial therapy within 48 to 72 hours and the absence of a deep-tissue infection, even in a patient with neutropenia. However, a recent study suggested that catheter-related BSIs resulting from *S aureus* in patients with cancer (including neutropenic patients) may improve with durations of therapy that are longer than 2 weeks because of the increased risk of complications with shorter treatment courses.¹⁰⁵ Catheter-related BSIs resulting from any pathogen that are complicated by disseminated or deep infection require at least 4 to 6 weeks of antimicrobial therapy.^{44,100}

Thrombosis

In 2007, ASCO published a guideline addressing the many issues related to venous thromboembolism in patients with cancer: Clinical Practice Guideline Recommendations for Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer.¹⁰⁶ CVC-associated thrombosis was not considered in that guideline. This guideline is currently being updated. Thrombosis associated with a CVC can involve the catheter tip, the length of the catheter, or the catheterized vessel in the upper limb, with or without involvement of the central vasculature of the neck or mediastinum.

The incidence of catheter-related thrombosis (symptomatic and asymptomatic) in patients with cancer varies considerably, ranging as high as 27% to 66% in adults⁷ and 50% in children.¹⁰⁷ The variation is in part related to the different techniques (eg, venography, ultrasonography) used to assess catheter-associated clots, differing definitions

of thrombosis, and varying study designs. In one systematic review, the rates of symptomatic thrombosis were between 0.3% and 28.6%,⁷ whereas another review found that on average, 12% of CVC thrombosis events were symptomatic.⁸ In more recent years, however, lower rates of symptomatic CVC-related venous thrombosis in the range of 4% to 8% have been reported.^{10,108,109} The reasons for this decrease are unclear, but it has been suggested that improvement in catheter materials, better insertion practices, and better catheter maintenance are contributory. Malpositioning of the catheter tip can cause difficulties with blood withdrawal and contribute to catheter occlusion. A catheter that is too short increases the risk of thrombosis; therefore, proper insertion technique and confirmation of catheter tip placement are important. Clinical symptoms of CVC-related thrombosis include edema, pain, and erythema of the affected limb, which can develop acutely or over a more prolonged period of time. With upper-extremity catheters, there may be swelling of the neck, supraclavicular area, or face. Often, problems with catheter function can lead to ultrasound or radiographic evaluations, which identify catheter-associated clots.

Clinical Question 4

What is effective prophylaxis for the prevention of catheter-related thrombosis?

Recommendation 4.1. The use of systemic anticoagulation (warfarin, low-molecular weight heparin [LMWH], or unfractionated heparin) has not been shown to decrease the incidence of catheter-associated thrombosis, and therefore, routine prophylaxis with anticoagulants is not recommended for patients with cancer with CVCs. Routine flushing with saline of the CVC to prevent fibrin buildup is recommended.

Literature review and analysis. Older studies produced conflicting conclusions regarding the efficacy of routine primary thromboprophylaxis in patients with cancer. Two small RCTs^{110,111} evaluated the use of low-dose warfarin and LMWH to prevent catheter-related thrombosis. Although in retrospect, there were many methodologic issues with the first study,¹¹⁰ the use of low-dose warfarin became common in some clinical practices. It was noted subsequently that the prothrombin time could be prolonged excessively in some patients because of interactions with chemotherapy drugs.¹¹²

More recently, 10 randomized trials, three systematic reviews, and one meta-analysis have addressed the routine use of thromboprophylaxis using a variety of different anticoagulants in a variety of different populations of patients with cancer.¹¹³⁻¹²⁶ Details of these articles are provided in the evidence tables in Data Supplements 1 and 2 at www.asco.org/guidelines/cvc. The use of anticoagulants did not increase the risk of bleeding, although bleeding certainly remains a concern in patients receiving intensely myelosuppressive therapy. More importantly, the systematic reviews and meta-analysis did not show a decrease in the incidence of symptomatic CVC-related thrombosis, and hence, the systemic administration of anticoagulants to prevent CVC-associated thromboses is not recommended.

There are a number of reasons that may explain the differences in event rates of contemporary compared with earlier studies. First, earlier trials were not double blinded and may have overestimated the treatment effects because of possible biases in diagnosis. Second, improvements in biocompatibility, insertion, and maintenance techniques for CVCs have helped to lower thrombosis rate in recent years, necessitating large trials to detect differences. Third, the patient pop-

ulations may have been different in the earlier trials. A number of new antithrombotic agents are undergoing clinical investigation or are in the pipeline, but more highly powered RCTs of better design are needed to define whether specific subgroups of patients with cancer might benefit from receiving thromboprophylaxis.

A special note is warranted for Factor V Leiden. A meta-analysis¹²⁷ of 10 studies was published on 1,000 patients with cancer with Factor V Leiden and the G20210A prothrombin mutation (PTM). The pooled OR for CVC-related thrombosis was 4.6 (95% CI, 2.6 to 8.1) in patients with Factor V Leiden compared with those without. The pooled OR for CVC-related thrombosis was 4.9 (95% CI, 1.7 to 14.3) in patients with PTM. The estimated attributable risk of CVC-related thrombosis was 13.1% for Factor V Leiden. They concluded that the presence of Factor V Leiden and PTM is associated with CVC-related thrombosis. However, Factor V Leiden and the prothrombin gene mutation were not associated with an increased risk of catheter-associated thrombosis in another study.¹²⁸ The study also described an increased risk of catheter-associated thrombosis with elevated homocysteine levels. Overall, there is no clear consensus at this time regarding the role of either inherited or acquired thrombophilic states in the pathogenesis of catheter-associated thrombosis, nor is there a clear recommendation on the use of prophylactic measures in this population.

Recommendation 4.2. Data are insufficient to recommend routine use of urokinase (not currently available in the United States) and/or other thrombolytics to prevent catheter occlusion.

Literature review and analysis. Three RCTs have evaluated methods to decrease the risk of CVC occlusion by flushing with urokinase in a variety of patient populations, and the conclusions are mixed. In two of the three studies,^{129,130} patients receiving urokinase had fewer occlusive events (23% v 31%; $P = .02$ and 4% v 16%; $P < .05$). In contrast, another study¹³¹ did not report any benefit of prophylactic urokinase in a trial of 100 patients undergoing bone marrow transplantation (including a large number of patients undergoing autologous transplantation for breast cancer) or receiving high-dose chemotherapy for hematologic malignancies. The incidence of catheter-related thrombosis was also similar in both groups, with 16% of the heparin group and 19% of the urokinase group developing a symptomatic upper-extremity deep venous thrombosis. One of the studies was closed early because of withdrawal of urokinase in the United States; nonetheless, it was determined that there were no significant differences in occlusive events with urokinase versus heparin instillation.¹²⁹

It is not clear why the incidence of catheter occlusion was different among the three RCTs, although the patient populations varied, and the definition and diagnosis of catheter occlusion differed. On the basis of both the lack of solid evidence and the unavailability of the agent in the United States, it is not possible for the Panel to recommend urokinase prophylaxis to prevent catheter occlusion.

Two other RCTs examined alternative interventions to prevent thrombotic events. One study¹³² found that ionic implantation of silicone chronic venous access devices did not alter thrombotic complications in a double-blinded, randomized clinical trial, whereas another small, and probably underpowered, study¹³³ suggested that a novel silver-coated CVC did not affect the rate of CVC-related thrombosis.

Management of Catheter-Related Occlusion

Clinical Question 5

What are effective treatments for the management of catheter-related occlusions?

Recommendation 5.1. The instillation of 2-mg t-PA is recommended to restore patency and preserve catheter function.

Literature review and analysis. Four RCTs¹³⁴⁻¹³⁷ have evaluated methods of restoring line patency using fibrinolytic therapy (alteplase [t-PA], reteplase, or tenecteplase), urokinase with t-PA, or urokinase with heparin (urokinase unavailable in the United States) for catheter occlusions. Most cancer centers have standard policies and procedures to treat asymptomatic CVC occlusions¹³⁸ with thrombolytic drugs. Although more studies are needed to establish a consensus for treatment of asymptomatic CVC-related thrombosis,¹³⁹ most are often diagnosed incidentally by cancer staging studies. Current data suggest that the treatment of incidental thrombi should be the same as treatment of symptomatic thrombi. These issues will be addressed in more detail in the forthcoming update (manuscript submitted, Lyman et al: Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update).

Recommendation 5.2. Although it is appropriate to try to clear a thrombosis with the CVC in place, if there is radiologically confirmed thrombosis that does not respond to fibrinolytic therapy or if fibrinolytic or anticoagulation therapy is contraindicated, catheter removal is recommended. Prolonged retention of an unneeded CVC can lead to significant problems associated with thrombosis and fibrosis. Three to 6 months of anticoagulant therapy with LMWH or LMWH followed by warfarin (international normalized ratio, 2.0 to 3.0) is recommended for the treatment of symptomatic CVC thrombosis, with the duration depending on clinical issues in individual patients.

Literature review and analysis. There are no randomized trials of anticoagulant therapy in patients with acute symptomatic CVC thrombosis. The natural history of acute CVC thrombosis is unclear. Although pulmonary embolism can occur,¹⁴⁰ the incidence is less frequent than that of proximal deep vein thrombosis of the leg. Treatment of this condition is based on extrapolation of the results of acute deep leg vein thrombosis. The duration of anticoagulation therapy is unclear, but 3 to 6 months seems reasonable. It is possible (even likely) that the duration of anticoagulation can be shorter if the catheter has been removed. Additional clinical issues, such as the planned administration of intensive chemotherapy that will produce thrombocytopenia, should be considered in individual patients.

The timing of the removal of a CVC because of a CVC-related thrombosis is unclear. It is the expert opinion of the CVC Care Panel that it may not always be necessary to remove the catheter in patients with CVC-associated thrombosis. One alternative is to keep the CVC in place and to add systemic anticoagulants, but there are no RCTs addressing this issue. For patients with deep vein thrombi for whom there are contraindications for anticoagulation, such as those with active bleeding, platelet count < 50,000/ μ L, or recent CNS bleeding or surgery, catheter removal is recommended, and anticoagulation therapy should be initiated if and/or when it becomes possible. Patients with cancer who have had their CVCs removed and then replaced without anticoagulation often experience recurrent thrombosis, but this has not been sufficiently studied. An important issue that needs to be studied is where to put the next CVC. Future research questions should include analyses of the development of postphlebotic syn-

drome, the importance and value of testing for thrombophilia and inherited disorders such as Factor V Leiden in patients who experience thromboses, and the management of small pericatheter clots detected by imaging studies in otherwise asymptomatic patients. Other ideas for future research on CVC care for patients with cancer are available in Data Supplement 8 at www.asco.org/guidelines.cvc.

PATIENT AND CLINICIAN COMMUNICATION

Adequate vascular access is critical for the patient with cancer and should be included in the patient assessment when making treatment decisions. Many CVCs are available; however, there is no evidence-based guideline for the selection of a particular CVC for each patient situation. Therefore, it is important for the oncologist to discuss CVC options, including risks and benefits, with the patient. It is important to explain to the patient that a central line may be inserted for one or more of the following reasons:

- Some chemotherapy drugs are not suitable to be administered into small veins in the hand or arm and must be administered in a larger vein for adequate dilution
- To allow some chemotherapy treatments, such as those administered by continuous infusion, to be administered at home and not require a lengthy hospital stay
- When extended chemotherapy treatments and frequent needle sticks to obtain blood samples are anticipated
- When a patient is felt to have poor venous access in the hands and arms not suitable for treatment infusions
- When a patient verbalizes or displays anxiety regarding needle sticks

When the oncologist and other practitioners determine that a CVC is required, it should be explained that a central line is a long narrow hollow tube made of soft plastic, which provides access to a large vein in the chest. The entrance location of the catheter is dependent on the type of central line, including tunneled, implanted, and PICC. Long-term CVCs can be used for medication administration, blood products, total parenteral nutrition, and blood drawing. Patients and caregivers of outpatients should be instructed about how to monitor for infection at the entrance-exit sites and to report other signs of infection or thrombosis such as fever or pain. The patient should be informed about his or her catheter, as follows:

Types of Catheters

Nontunneled catheters. When these catheters are used, they are most commonly placed into the subclavian vein (under the collar bone) or internal jugular vein in the neck. With proper care from a dedicated team, these catheters can facilitate the administration of fluids and chemotherapy as well as the drawing of blood samples, often for the entire duration of therapy. These will require sutures at the site where the catheter exits the skin. These catheters do not require that a patient go to the operating room or have general anesthesia, and they can be removed easily when no longer needed. In urgent situations for short-term use, these catheters can be placed into the large veins of the neck or groin but should be removed as quickly as possible because they carry a higher risk of complications.

Tunneled catheters. Tunneled catheters, sometimes referred to as Hickman catheters, are inserted by puncturing the vein below the collar bone or lower neck (the insertion site) and secured by threading

the line under the skin, exiting above the nipple on the chest wall (the exit site). The line may have a small Dacron cuff around it that imbeds into the tissue in the skin tunnel to prevent it from falling out. A small cut is made at both the insertion and exit sites, requiring one or two stitches in each. The stitches are removed in approximately 3 weeks when the cuff is secure, and the skin has healed. No needle sticks are needed with this type of catheter. Complications may include infection or bleeding at the entrance-exit site or in the subcutaneous tunnel, blood clots in or around the catheter, lung collapse during insertion, and catheter occlusion.

Implanted catheters. The implantable catheter or port consists of a catheter attached to a reservoir that is implanted into a surgically created pocket on the chest wall or upper arm. A needle is inserted through the skin to the septum of the port to access the reservoir. Advantages of this type of catheter are reduced risk of infection, less frequent flushing, and less interference with daily activities. Complications may include infection of the port site or catheter, blood clots in or around the catheter, lung collapse during insertion, and catheter occlusion.

Peripherally Inserted Central Catheters. The PICC line is inserted into the upper arm veins and threaded into the larger veins in the chest. This catheter is intended for patients requiring up to 12 months of IV therapy. An advantage of this type of catheter is the lack of needle sticks and placement at the bedside. Disadvantages include more frequent flushing and dressing changes. Complications may include infection at the exit site, blood clots in or around the catheter, and catheter occlusion. Placement of these types of catheters above the antecubital fossa diminishes the likelihood of thrombophlebitis.

Reliable venous access is critical for the patient with cancer to prevent delays in treatment. Effective communication among the oncologist, the individuals placing the venous access device, and most importantly the patient during the treatment-planning phase will promote improved patient outcomes. More patient information about CVCs in cancer treatment, including information about monitoring and caring for catheters at home, can be found at www.cancer.net, specifically www.cancer.net/patient/All+About+Cancer/Cancer.Net+Feature+Articles/Treatments%2C+Tests%2C+and+Procedures/Catheters+and+Ports+in+Cancer+Treatment.

HEALTH DISPARITIES

Although ASCO clinical practice guidelines represent expert recommendations on the best practices in disease management to

provide the highest level of cancer care, it is important to note that many patients have limited access to medical care. Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Racial/ethnic minority patients with cancer suffer disproportionately from comorbidities, can experience substantial obstacles to receiving care, are more likely to be uninsured, and are at greater risk of receiving poorer quality care than other Americans.¹⁴¹⁻¹⁴⁴ Many other patients lack access to care because they live at a distance from appropriate treatment facilities.

Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations. In particular, the availability of adequate home care for catheter maintenance might vary widely among different patient populations and could influence the choice of CVC. The role of the oncologist/hematologist in guiding patient decisions should not be minimized. Furthermore, although in the overall scheme of a patient's care, the placement of a venous access device may seem minor, it can present difficulties that can dramatically affect a patient's ability to receive appropriate treatment.

ADDITIONAL RESOURCES

Data supplements, including evidence tables, and clinical tools and resources can be found at www.asco.org/guidelines/cvc. Patient information is available at www.cancer.net.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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Appendix

Table A1. CVC Care Panel Members

Panel Member	Affiliation/Institution
Charles A. Schiffer, chair	Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI
Mark N. Levine, co-chair	Henderson Hospital, Hamilton, Ontario, Canada
James C. Wade, co-chair	Geisinger Cancer Institute, Danville, PA
Dawn Camp-Sorrell	University of Alabama, Birmingham, AL
Diane G. Cope	Florida Cancer Specialists and Research Institute, Fort Myers, FL
Bassel F. El-Rayes	Emory University, Atlanta, GA
Barry Feig	University of Texas, MD Anderson Cancer Center, Houston, TX
Mark Gorman	Patient Representative, Silver Spring, MD
Jennifer Ligibel	Dana-Farber Cancer Institute, Boston, MA
Paul Mansfield	University of Texas MD Anderson Cancer Center, Houston, TX
Mary Mulcahy	Northwestern University School of Medicine, Chicago, IL

Abbreviation: CVC, central venous catheter.