ACR Appropriateness Criteria® Radiologic Management of Central Venous Access

Expert Panel on Interventional Radiology: *Colette M. Shaw, MB[a], Shrenik Shah, MD[b], Baljendra S. Kapoor, MB, BS[c], Thomas R. Cain, MD[d], Drew M. Caplin, MD[e], Khashayar Farsad, MD, PhD[f], M-Grace Knuttinen, MD, PhD[g], Margaret H. Lee, MD[h], Joseph J. McBride, MD[i], Jeet Minocha, MD[j], Elizabeth V. Robilotti, MD, MPH[k], Paul J. Rochon, MD[l], Richard Strax, MD[m], Elrond Y. L. Teo, MD[n], Jonathan M. Lorenz, MD[o]*

Abstract

Obtaining central venous access is one of the most commonly performed procedures in hospital settings. Multiple devices such as peripherally inserted central venous catheters, tunneled central venous catheters (eg, Hohn catheter, Hickman catheter, C. R. Bard, Inc, Salt Lake City UT), and implantable ports are available for this purpose. The device selected for central venous access depends on the clinical indication, duration of the treatment, and associated comorbidities. It is important for health care providers to familiarize themselves with the types of central venous catheters available, including information about their indications, contraindications, and potential complications, especially the management of catheters in the setting of catheter-related bloodstream infections.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment.

Key Words: Appropriateness Criteria, Appropriate Use Criteria, AUC, Catheter, Central venous, Nontunneled, PICC, Port, Tunneled

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[a]Principal Author, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

[b]Research Author, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

[c]Panel Chair, Cleveland Clinic, Cleveland, Ohio.

[d]Yuma Regional Medical Center, Yuma, Arizona.

[e]Hofstra Northwell School of Medicine, Manhasset, New York.

[f]Oregon Health and Science University, Portland Oregon.

[g]Mayo Clinic, Phoenix, Arizona.

[h]David Geffen School of Medicine at UCLA, Los Angeles, California.

[i]University of Nebraska Medical Center, Omaha, Nebraska.

[j]University of California San Diego, San Diego, California.

[k]Memorial Sloan Kettering Cancer Center, New York, New York; Infectious Diseases Society of America.

[l]University of Colorado Denver, Anschutz Medical Campus, Aurora, Colorado.

[m]Baylor College of Medicine, Houston, Texas.

[n]Emory University School of Medicine, Atlanta, Georgia; Society of Critical Care Medicine.

[o]Specialty Chair, University of Chicago Hospital, Chicago, Illinois.

Corresponding author: Colette M. Shaw, MB, Thomas Jefferson University Hospital, Attn: Division of Interventional Radiology, 766 Main Bldg, 132 S 10th St, Philadelphia, PA 19107-5244; e-mail: colette.shaw@jefferson.edu.

Disclaimer: The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

ACR Appropriateness Criteria® Radiologic Management of Central Venous Access. Variants 1 to 14 and Table 1.

Variant 1. Device selection. Adult or child ≥ 13 years of age. Intravenous access for long-term total parenteral nutrition and intermittent intravenous antibiotics.

Treatment/Procedure	Appropriateness Category
Chest port	Usually Appropriate
Arm port	May Be Appropriate
Single lumen PICC	Usually Not Appropriate
Double lumen PICC	May Be Appropriate
Tunneled small bore central venous catheter single lumen	May Be Appropriate
Tunneled small bore central venous catheter double lumen	Usually Appropriate

PICC = peripherally inserted central catheter.

Variant 2. Device selection. Adult or child ≥ 13 years of age. Sickle cell anemia requires intravenous access for the treatment of recurrent sickle cell crisis.

Treatment/Procedure	Appropriateness Category
Chest port	Usually Appropriate
Arm port	May Be Appropriate
Single lumen PICC	May Be Appropriate
Double lumen PICC	May Be Appropriate
Tunneled central venous catheter	May Be Appropriate
Nontunneled central venous catheter	May Be Appropriate

PICC = peripherally inserted central catheter.

Variant 3. Device selection. Adult or child ≥ 13 years of age. Stage 3 chronic kidney disease requires central venous access for 6 weeks of antibiotic treatment.

Treatment/Procedure	Appropriateness Category
Chest port	Usually Not Appropriate
Arm port	Usually Not Appropriate
Single lumen PICC	Usually Not Appropriate
Double lumen PICC	Usually Not Appropriate
Tunneled small bore central venous catheter single lumen	Usually Appropriate
Tunneled small bore central venous catheter double lumen	May Be Appropriate

PICC = peripherally inserted central catheter.

Variant 4. Device selection. Adult or child ≥ 13 years of age. Intensive care unit (ICU) patient with sepsis and acute renal insufficiency requires intravenous access for approximately 7 to 10 days.

Treatment/Procedure	Appropriateness Category
Chest port	Usually Not Appropriate
PICC	May Be Appropriate
Tunneled small bore central venous catheter	Usually Not Appropriate
Nontunneled central venous catheter	Usually Appropriate

PICC = peripherally inserted central catheter.

Variant 5. Site selection. Adult or child ≥ 13 years of age. Head and neck surgery. Central venous access required for adjuvant chemotherapy.

Treatment/Procedure	Appropriateness Category
Arm port	Usually Appropriate
PICC	Usually Appropriate
Chest port via internal jugular/subclavian vein	Usually Appropriate
Tunneled small bore catheter via internal jugular/subclavian vein	May Be Appropriate

PICC = peripherally inserted central catheter.

Variant 6. Site selection. Adult or child ≥ 13 years of age. Sepsis in a patient with stage 4 chronic kidney disease, requires 7 to 10 days of intravenous antibiotic therapy.

Treatment/Procedure	Appropriateness Category
PICC	Usually Not Appropriate
Nontunneled central venous catheter via the left internal jugular vein	Usually Appropriate
Nontunneled central venous catheter via the right internal jugular vein	Usually Appropriate
Nontunneled central venous catheter via the subclavian vein	Usually Not Appropriate

PICC = peripherally inserted central catheter.

Variant 7. Site selection. Adult or child ≥ 13 years of age. ICU patient with sepsis. The patient receives hemodialysis via nontunneled catheter placed via the right internal jugular vein. Multilumen central venous access required.

Treatment/Procedure	Appropriateness Category
Arm PICC	Usually Not Appropriate
Femoral vein nontunneled central venous catheter	May Be Appropriate
Right internal jugular vein nontunneled central venous catheter	Usually Appropriate
Subclavian vein nontunneled central venous catheter	May Be Appropriate
Left internal jugular vein nontunneled central venous catheter	Usually Appropriate

ICU = intensive care unit; PICC = peripherally inserted central catheter.

Variant 8. Site selection for permanent hemodialysis catheter. Adult or child ≥ 13 years of age. End-stage renal disease has undergone creation of a left arm arteriovenous fistula. The fistula has not yet matured.

Treatment/Procedure	Appropriateness Category
Right internal jugular vein	Usually Appropriate
Right subclavian vein	May Be Appropriate
Left internal jugular vein	May Be Appropriate
Left subclavian vein	Usually Not Appropriate
Right or left femoral vein	May Be Appropriate

Variant 9. Immunocompromised patient. Adult or child ≥ 13 years of age. Has a tunneled small-bore catheter placed via right internal jugular vein. Patient is pancytopenic (ANC 300/μL, PLT 32,000/μL) and presents with fevers and malaise.

Treatment/Procedure	Appropriateness Category
Immediate removal of the tunneled catheter, culture of the catheter tip and placement of a nontunneled central venous catheter via different site	May Be Appropriate
Retain the catheter and commence empiric antibiotics once peripheral and central blood cultures have been drawn	May Be Appropriate
Catheter should be removed if positive blood cultures are confirmed	Usually Appropriate
Catheter salvage may be considered even after positive blood cultures are acquired	May Be Appropriate

ANC = absolute neutrophil count; PLT = platelet count.

Variant 10. Thrombotic complications. Adult or child ≥ 13 years of age. Chest port placed via right internal jugular vein is being used for chemotherapy. The infusion nurse can infuse saline but is unable to aspirate blood from the catheter.

Treatment/Procedure	Appropriateness Category
Continue to use the port for administering drugs but use peripheral access for blood draws	May Be Appropriate
Catheter removal and placement of alternative venous access	May Be Appropriate
Chest radiograph	Usually Appropriate
Interrogate the port with patient and/or patient arm in different positions	Usually Appropriate
Instill a thrombolytic agent into the port	Usually Appropriate
Contrast study of the catheter	Usually Appropriate
Catheter exchange	May Be Appropriate
Catheter stripping	May Be Appropriate

Variant 11. Thrombotic complications. Adult or child ≥ 13 years of age. Permanent hemodialysis catheter placed via the right internal jugular vein. Poor flows are documented at hemodialysis via both lumens.

Treatment/Procedure	Appropriateness Category
Catheter removal and placement of a new catheter from a different site	Usually Appropriate
Catheter exchange	Usually Appropriate
Contrast study of the catheter	Usually Appropriate
Fibrin sheath stripping	Usually Appropriate
Fibrin sheath disruption	Usually Appropriate
Attempt to perform dialysis with patient arm in a different position	Usually Appropriate

Variant 12. Thrombotic complications. Adult or child ≥ 13 years of age. Arm swelling secondary to extensive thrombus surrounding a triple lumen PICC placed via left basilic vein. The catheter is being used for long-term parenteral nutrition and intermittent intravenous antibiotics. The catheter is functioning.

Treatment/Procedure	Appropriateness Category
Immediate catheter removal	May Be Appropriate
Commence anticoagulation and continue to use the catheter	Usually Appropriate
Catheter-directed thrombolysis	May Be Appropriate
Systemic thrombolysis	Usually Not Appropriate
SVC filter placement	Usually Not Appropriate
Catheter downsize for a single/double lumen PICC	Usually Not Appropriate

PICC = peripherally inserted central catheter; SVC = superior vena cava.

Variant 13. Infectious complications. Adult or child ≥ 13 years of age. Preventive measures to reduce catheter-related bloodstream infections when placing a nontunneled central venous catheter in ICU patient.

Treatment/Procedure	Appropriateness Category
Antibiotic impregnated catheters	May Be Appropriate
Upper body insertion site	Usually Appropriate
Heparin-bonded catheter	May Be Appropriate
Prophylactic antibiotics prior to catheter placement	May Be Appropriate
Antimicrobial lock therapy (not ethanol lock)	May Be Appropriate
Routine guide-wire catheter exchanges	Usually Not Appropriate

ICU = intensive care unit.

Variant 14. Infectious complications. Adult or child ≥ 13 years of age. Therapeutic measures to manage catheter-related bloodstream infections.

Treatment/Procedure	Appropriateness Category
Catheter should be removed immediately	May Be Appropriate
Catheter should be removed in the setting of Staphylococcus Aureus bacteremia	Usually Appropriate
Catheter should be preserved in clinically stable patients	May Be Appropriate
Catheter exchange in conjunction with systemic antibiotics can be considered in patients with coagulase-negative Staphylococcal bacteremia	May Be Appropriate
Exit site infections may be treated with antibiotics alone	May Be Appropriate
Catheter salvage and concomitant antibiotic therapy are appropriate in patients with limited venous access	Usually Appropriate

Table 1. Appropriateness category names and definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

SUMMARY OF LITERATURE REVIEW

Introduction/Background

Image-guided percutaneous central venous (CV) access refers to the use of real-time imaging (fluoroscopy and/or sonography) to place a catheter in a vein that leads directly to the heart. The catheter tip is positioned at the cavo-atrial junction, or in the right atrium. Central venous catheters (CVCs) include peripherally inserted central catheters (PICC), temporary (nontunneled) CVCs, long-term (tunneled) CVCs, and totally implantable devices. CV access may be required for diagnostic and/or therapeutic reasons. Many of the indications for CV access are not mutually exclusive to a particular device. Diagnostic indications include establishing and/or confirming a diagnosis, establishing a prognosis, monitoring a response to treatment, and repeated blood sampling. Therapeutic indications include administration of chemotherapy, parenteral nutrition (PN), blood products, intravenous medications or fluids, and performance of plasmapheresis or hemodialysis [1].

Radiologically guided percutaneous insertion is associated with higher technical success rates, fewer complications, shortened procedure times, and subsequent reduction in costs compared with other specialties [2-6].

DISCUSSION BY VARIANT

Variant 1: Device selection. Adult or child ≥ 13 years of age. Intravenous access for long-term total parenteral nutrition and intermittent intravenous antibiotics

Variant 2: Device selection. Adult or child ≥ 13 years of age. Sickle cell anemia requires intravenous access for the treatment of recurrent sickle cell crisis

Variant 3: Device selection. Adult or child ≥ 13 years of age. Stage 3 chronic kidney disease requires central venous access for 6 weeks of antibiotic treatment

Variant 4: Device selection. Adult or child ≥ 13 years of age. Intensive care unit (ICU) patient with sepsis and acute renal insufficiency requires intravenous access for approximately 7 to 10 days

The ideal CV access device should be radiopaque, hemocompatible, and durable. The catheter and the vein

in which it is placed should allow brisk infusion and easy aspiration of fluids. Patient comfort and mobility should not be adversely affected. There is no evidence-based guide to the selection of the most appropriate CV access device for each clinical situation. Device selection is determined by several factors: the patient's diagnosis and clinical status; the type, frequency, and duration of therapy; the patient's history of CV access and patency of the access veins; patient preference; and operator experience.

Duration of Therapy. Short-term (1-3 weeks) CVCs are nontunneled (temporary) 20- to 30-cm-long catheters inserted into a central vein (subclavian, internal jugular, innominate, axillary, or femoral vein). They may have a single or multiple lumens and range in size from 5F to 14F. They are designed for continuous short-term (1-3 weeks) infusions, drug delivery, hemodialysis, apheresis, and CV pressure monitoring.

Intermediate (<3 months) CVCs are nontunneled devices specifically designed for prolonged intermittent use, such as PICCs and Hohn catheters. PICCs are nontunneled, central catheters inserted through a peripheral vein of the arm. They range from 2F to 7F, and may have one, two, or three lumens. The catheter extends from the puncture site to the superior vena cava (SVC). Hohn catheters are nontunneled, 20-cm-long, centrally inserted catheters. They are available as either single lumen 5F or dual lumen 7F. The catheter is made of silicone and has a nontapered tip. Both PICCs and Hohn catheters can be used for prolonged continuous or intermittent infusion therapies (up to 3 months) both in hospitalized patients and in outpatients.

Long-term (>3 months) CVCs include tunneled CVC or a totally implanted port. Tunneled catheters travel through a short (8-15 cm) subcutaneous tunnel before entry into an accessed vein. Sizes range from 3.5F to 21F. The cuff induces an inflammatory reaction within the subcutaneous tunnel, leading to fibrosis and consequent catheter fixation, usually within 3 to 4 weeks after insertion. The cuff also inhibits migration of organisms into the catheter tract, thus reducing infection rates compared with temporary catheters. Totally implanted ports consist of a reservoir connected to a CVC, which may or may not be valved. The reservoir is implanted in the chest or arm. Ports have lower reported rates of catheter-related bloodstream infections (CRBSIs) than both tunneled and nontunneled CVCs [7]. Tunneled CVC is recommended for patients requiring continuous access, whereas a totally implantable access device should be reserved for patients who require long-term, intermittent vascular access.

Catheter Design. The materials used to make the catheter and the catheter design have undergone considerable modifications to improve function and reduce catheter-related complications.

Catheter Size and Number of Lumens. In general, the smallest diameter catheter and minimum number of lumens should be used to minimize the risk of catheter-related complications [8,9]. Multilumen catheters may be used when multiple simultaneous therapies are required or when infusion of noncompatible medications and fluids require additional venous access. In patients with chest ports who require higher infusion rates, the flow through a catheter 6F or greater will be limited by the size of the accessing Huber needle used and not the catheter lumen. In patients who require PN, it is generally recommended that a single lumen be dedicated exclusively to that purpose [10].

Materials. The properties of the catheter material can impact device placement and performance in several ways. Almost all CVCs are now made of silicone or polyurethane. These materials have been associated with fewer infections than polyvinyl chloride or polyethylene [11,12]. Silicone, a soft biocompatible rubber, is one of the least traumatic and thrombogenic materials available. Silicone catheters are more prone to compression and "pinch off." Polyurethane, on the other hand, is a tougher and stiffer material. Greater catheter stiffness and size are associated with an increased risk of mechanical phlebitis. In general, silicone is more compatible with infusates, and polyurethane is more susceptible to degradation by various drug solvents [13].

In an attempt to reduce catheter-related complications, catheters and cuffs that are coated or impregnated with antimicrobial, antiseptic, or antithrombotic agents have been developed. The data available relates primarily to triple lumen, temporary catheters in adult patients with catheter dwell time <30 days. Two meta-analyses of first-generation catheters coated externally with chlorhexidine and silver showed a reduced risk for CRBSI compared with standard noncoated catheters [14,15]. Three prospective, randomized studies of second-generation catheters demonstrated a significant reduction in catheter colonization but were underpowered to show a difference in CRBSI [16-18]. CVCs impregnated on both the external and internal surfaces with minocycline and rifampin

were associated with lower rates of CRBSI when compared with the first-generation chlorhexidine- and silver sulfadiazine-impregnated catheters [19]. The beneficial effect began after day 6 of catheterization. Silicone minocycline- and rifampin-impregnated CVCs with an average dwell time of over 60 days have been shown to be effective in reducing CRBSI [20]. Conflicting results have been obtained from a number of prospective randomized controlled trials (RCTs) comparing platinum- and silver-impregnated catheters with nonimpregnated catheters [21-23]. In 2011, the US Centers for Disease Control and Prevention (CDC) recommended the use of a chlorhexidine- and silver sulfadiazine- or minocycline- and rifampin-impregnated CVC in patients whose catheter is expected to remain in place more than 5 days if, after successful implementation of a comprehensive strategy to reduce rates of catheter-line–associated bloodstream infection, the infection rate is not decreasing [24].

Thrombolytic coatings (eg, heparin) have been incorporated into the design of some tunneled catheters. A retrospective comparison of heparin-coated and non-coated hemodialysis catheters showed a significantly lower risk of catheter-related bacteremia among the heparin-coated catheters, but the coating did not decrease the risk of catheter malfunction [25]. The longevity of the coatings, the risk of antibiotic resistance, and the safety of the antithrombotic coatings, particularly in patients who may be heparin-induced thrombocytopenia positive, need to be assessed. At present, there is inadequate evidence to support the use of PICCs or tunneled catheters coated with anti-infective or antithrombotic drugs.

Catheter Tip Design. Numerous catheter tip designs exist, including end-hole, valved tip, and staggered tips. End-hole is the tip configuration in most temporary catheters and can be cut to the appropriate length. Valved-tip catheters have a closed blunt tip with valved slits just proximal to the tip. Although infusion and aspiration are possible, the tip prevents blood from entering the lumen when not in use, obviating the need for heparin flushes. Because the tip cannot be modified, the catheter length is trimmed at the hub. In an RCT, they were not superior to a traditional, open-ended device in terms of catheter efficacy and early and late complications [26].

Hemodialysis and apheresis require flow rates of approximately 350 and 125 cc/min, respectively. Hemodialysis catheter tip designs include a single catheter with two lumens and a central septum (eg, Optiflow, Fisher & Paykel Healthcare Limited; Hickman catheters,

C. R. Bard, Inc, Salt Lake City UT), two distinct circular lumens (eg, PermCath catheter, Sherwood Medical, St. Louis, MO), two distinct catheters partially attached (eg, Ash Split catheter, Medcomp, Harleysville, PA), and two distinct and separate catheters (eg, Tesio catheter, Medcomp, Harleysville, PA). In most designs, the distal catheter tips are staggered to prevent recirculation; typically, the venous port is more inferior. Currently, there is insufficient evidence to support one type of hemodialysis catheter design over another [27-30].

Indication for Use. *Hemodialysis.* The vascular access of choice for maintenance hemodialysis is the native arteriovenous fistula. Hemodialysis access of <3 weeks' duration should be obtained using a noncuffed, or a cuffed, double-lumen percutaneously inserted catheter. Noncuffed femoral catheters should not be left in place longer than 5 days and should be left in place only in bed-bound patients. Tunneled cuffed venous catheters are the method of choice for temporary access of >3 weeks' duration. Some patients who have depleted all other access options require permanent access via tunneled cuffed catheters. For patients who have a primary arteriovenous fistula maturing but need immediate hemodialysis, tunneled cuffed catheters are the access of choice.

The National Kidney Foundation Disease Outcomes Quality Initiative (NKF-KDOQI) Clinical Practice Guidelines for Vascular Access currently recommends restricting venous access for patients with chronic kidney disease stage 3 or worse [31]. The NKF-KDOQI guidelines recommend the use of small-bore catheters placed via the internal jugular vein and avoidance of the subclavian vein when CV access is indicated in patients with stage 3 to 5 chronic kidney disease. In general, a PICC line should not be placed in patients at risk for future hemodialysis vascular access.

PN. CV access, which allows delivery of nutrients directly into the SVC or the right atrium, is needed in most patients who are candidates for PN. It is recommended that peripheral PN delivered via short or midline catheters should be used only for a limited period of time, and only for nutrient solutions with osmolarity of 850 mOsm/L or less [32]. For high osmolarity PN, the tip of the catheter should be placed in the lower third of the SVC or in the upper right atrium to avoid injury to the endothelium of the veins. Both nontunneled CVCs and PICCs are suitable for short-term inpatient PN [33,34]. Neither device has been shown to be superior in this

patient population. For medium-term or home PN, PICCs, Hohn catheters, tunneled catheters, and ports are appropriate [35]. PICCs may not be suitable for patients receiving home PN who are self-caring because the PICC effectively disables one arm. For prolonged use and home PN for >3 months, a tunneled catheter or port is advised [36]. Venous ports have been recommended only for patients who require long-term, intermittent vascular access, and for patients requiring long-term frequent or continuous access, a tunneled CVC is preferable [1].

Chemotherapy. Oncology patients often require indefinite venous access that will serve them through all phases of their disease. There are very limited data to guide clinicians when selecting a device for their oncologic patient. CV access is recommended for the administration of boluses of vesicant drugs but is essential for continuous infusion of these agents. Although many clinical factors may impact the choice of device, patient involvement has been shown to result in greater patient satisfaction, fewer delays in therapy related to loss of vascular access, fewer device complications, preservation of peripheral veins, less nursing time spent attempting to gain vascular access, shorter hospital stays, fewer emergency room visits, and decreased infusion therapy costs [37].

Ports have been shown to have the lowest reported rates of CRBSI compared with either tunneled or non-tunneled CVCs [38]. The only study to randomize patients with solid tumors commencing chemotherapy to surgical port placement versus standard peripheral venous access showed low port complication rates (0.23 per 1,000 days of use) and significantly less access-related anxiety and pain with 27% of the control group ultimately requiring CV access [39]. Costs were considerably higher in the port group compared with controls. Although overall quality of life scores was comparable in the two groups, the study had limited power to detect significant differences in the subscale sores.

Single lumen ports are ideally suited to patients with solid tumors receiving long-term intermittent bolus chemotherapy. Double lumen ports may be required in oncologic patients who require regular blood transfusions or bone marrow transplantation or for the administration of noncompatible infusates. Port implantation in brachial veins is associated with easy vascular access and a lower risk of complications at insertion. They may be preferable in patients with tracheostomy, head and neck tumors,

and anatomic deformities in the chest that may make access and nursing care more difficult. Kuriakose et al [40] reported more frequent thrombogenic complications in arm ports than in chest ports (11.4% versus 4.8% respectively).

Although medium- and long-term access devices are both acceptable in outpatients, PICCs have been associated with a higher incidence of thrombosis in patients with hematological and nonhematological malignancies [41]. This is an important consideration in patients who have had previous thromboses and in those who are receiving therapy, which may increase the thrombotic tendency. The risk of PICC-related venous thrombosis can be reduced by avoiding PICCs with calibers greater than 4F and by using ultrasound guidance for placement. A systematic review and meta-analysis including 5 RCTs and 25 observational studies comparing centrally inserted external catheters with totally implantable ports in patients undergoing chemotherapy showed a 3- to 4-fold increased risk of infections, noninfections complications, and device removal, compared with implantable ports [42].

Hospitalized Patients. Nontunneled CVCs are used for short-term venous access in the majority of hospitalized patients. A multicenter study analyzing 2,101 CVCs inserted in critically ill patients showed PICCs were associated with a significantly lower rate of bloodstream infection than standard CVCs [43]. No RCT has yet proven this. A meta-analysis from Turcotte et al [44] consisting of 48 studies published between 1979 and 2004 did not find clear evidence that PICC is superior to CVC in acute care settings. In this meta-analysis, infectious complications did not significantly differ between PICC and CVC; however, all PICC placements were performed without ultrasound guidance. In relation to PN in hospitalized patients, PICCs should be considered in patients with tracheostomy and in patients where insertion-related complications are increased (eg, patients with coagulation abnormalities) [10].

Variant 5: Site selection. Adult or child ≥ 13 years of age. Head and neck surgery. Central venous access required for adjuvant chemotherapy

Variant 6: Site selection. Adult or child ≥ 13 years of age. Sepsis in a patient with stage 4 chronic kidney disease, requires 7 to 10 days of intravenous antibiotic therapy

Variant 7: Site selection. Adult or child ≥ 13 years of age. ICU patient with sepsis. The patient receives hemodialysis via nontunneled catheter placed via the right internal jugular vein. Multilumen central venous access required

Variant 8: Site selection for permanent hemodialysis catheter. Adult or child ≥ 13 years of age. End-stage renal disease has undergone creation of a left arm arteriovenous fistula. The fistula has not yet matured

The risk of catheter-related complications varies according to the site of catheter insertion. Factors to consider when selecting the optimal insertion site include the presence of acute or chronic thrombus in the target vein, CV access history, and integrity of the surrounding soft tissues.

Peripheral Veins. CV access via peripheral vein may be preferable in a patient with a tracheostomy, severe anatomical abnormalities of neck and thorax, or marked thrombocytopenia and in patients who require home PN for limited periods of time.

In the upper limb, PICCs and subcutaneous arm ports are usually placed via the basilic, brachial, or cephalic veins when image guidance is employed. The basilic vein is the access vein of choice because it is superficial and is usually the largest vein in the arm. Access via the cephalic vein has a higher incidence of thrombosis. This is due to its smaller size and catheter susceptibility to movement and kinking as it overlies the biceps muscle. Brachial vein access carries a greater risk of injury to the brachial artery and median nerve.

Conventional Central Veins. Determination of the optimal site for CV access can be complex. The decision should be based on a careful evaluation of the relative risks and benefits of each site.

The femoral route is often preferred in emergency or high-risk situations (eg, severe thrombocytopenia or coagulopathy), where insertion complications are lower and hemostasis is easier to achieve. In patients in whom the internal jugular and subclavian veins are occluded or otherwise unavailable for puncture, or in the event of SVC obstruction, femoral vein access may also be considered. In 2011, the CDC advised against using femoral vein for CV access in adult patients [24]. This recommendation was based on studies that demonstrated high femoral catheter colonization rates compared with subclavian and internal jugular sites in adults and, in some studies, higher rates of CRBSI [45,46]. Femoral catheters were also associated with a higher risk of deep venous thrombosis (DVT) than internal jugular or subclavian catheters [47,48]. Femoral venous access should be avoided in patients with aortobifemoral bypass grafts or a femoral-distal bypass graft due to the risk of infection. The femoral vein is relatively contraindicated for PN due to the high risk of contamination at the groin exit site and the high risk of venous thrombosis. Tunneling onto the anterior abdominal wall can take the exit site out of the groin, thus facilitating access and nursing care. In 2012, a Cochrane review of CV access sites for prevention of thrombosis stenosis and infection reported lower risks of catheter colonization and thrombotic complication attributed to subclavian CV access compared with femoral CV access in short-term catheterizations [49]. A single randomized study of short-term hemodialysis catheterization in 293 critically ill patients reported higher risks of mechanical complications but equivalent infection risks from internal jugular CV access routes compared with femoral access [47]. Clinical interpretation of these results is limited due to the lack of ultrasound guidance used for the internal jugular vein access cases. Based on evidence from a number of observational studies in which nontunneled CVCs placed via jugular route were associated with higher colonization rates or CRBSI than those inserted into a subclavian vein, the CDC 2011 guidelines recommend placing nontunneled CVCs in adults at subclavian rather than jugular or femoral sites. This recommendation is supported by similar findings from a multicenter RCT involving 3,027 intensive care unit (ICU) patients [50].

Long-term catheterization data comparing subclavian and internal jugular CV access routes among 268 cancer patients showed similar risks for catheter-related complications [51]. Radiologists have used both the subclavian and internal jugular veins for chest port insertion [3,7]. Using ultrasound guidance, the internal jugular vein is easier to puncture than the subclavian vein and is the vessel of choice for CV access by interventional radiologists. The right internal jugular is preferred to the left because it has a relatively straight course, facilitating catheterization, and has a negligible risk of symptomatic CV stenosis and thrombosis. The incidence of CV thrombosis or stenosis for nontunneled catheters has been reported at 40% to 50% with the subclavian route versus 0% to 10% with the right internal jugular route [14,15]. Subclavian vein thrombosis can result in painful arm swelling that may necessitate catheter removal, anticoagulation therapy, or

thrombolysis. Other disadvantages of subclavian vein access include the higher risk of pneumothorax, catheter fatigue, pinch-off, and possibly fracture due to compression by the costoclavicular ligaments and subclavius muscle.

There are inadequate data relating to nonhemodialysis tunneled catheter placement to recommend a preferred site for access. In relation to long-term hemodialysis catheter placement, the NKF-KDOQI guidelines strongly recommend avoidance of the subclavian vein unless no other option exists or unless the ipsilateral extremity can no longer be used for permanent dialysis access [31]. The right internal jugular vein is the preferred access site because it has a more direct trajectory to the cavo-atrial junction and is associated with a lower risk of complications compared with other insertion sites [52]. Furthermore, placement via the left internal jugular vein may jeopardize the venous return from the left arm and rule out future fistula formation on that side. Catheter placement in the left internal jugular vein is associated with poor blood flow rates and high rates of stenosis and thrombosis [53]. If possible, the tunneled catheter should be placed on the contralateral side to a maturing fistula [31].

Unconventional Venous Access. The loss of CV access options in a patient requiring long-term hemodialysis or PN can be life-threatening. Alternative means of obtaining CV access include recanalization of occluded vein segments, use of collateral neck or chest veins, catheter placement in the inferior vena cava via infraumbilical, translumbar, or transhepatic approaches, and right atrial catheter placement via transhepatic venous approach.

Collateral neck or chest wall veins develop in response to chronic CV narrowing and occlusion. In patients with a well-established collateral network via mediastinal, intercostal, paraspinal, or azygos veins, access via these vessels is unlikely to result in symptomatic CV obstruction. Procedure-related complication rates are comparable to those via conventional venous access sites [54].

When all options for permanent catheter placement in the chest have been exhausted, femoral venous access or translumbar inferior vena cava access may be considered. Femoral vein access should not be used without first considering lower extremity fistula formation. Permanent femoral catheters are associated with a higher rate of infection and occlusion, resulting in more frequent interventions for catheter maintenance. Translumbar cava access is technically more challenging and time-consuming.

Infection rates for tunneled catheters are comparable with chest veins, but the risk of catheter malfunction is greater [55]. Transhepatic CV access is associated with a high risk of catheter malfunction due to constant catheter tip movement with respiration. In a review of 36 transhepatic CV access catheterizations, catheter occlusion was reported at 2.4 per 100 catheter-days [56].

Variant 9: Immunocompromised patient. Adult or child ≥ 13 years of age. Has a tunneled small-bore catheter placed via right internal jugular vein. Patient is pancytopenic (ANC 300/μL, PLT 32,000/μL) and presents with fevers and malaise

Acquired Immunodeficiency Syndrome. Increased susceptibility to opportunistic infections among acquired immunodeficiency syndrome (AIDS) patients is due to defective cell-mediated immunity, impaired B-cell antibody response, neutropenia (20% to 25% of AIDS sufferers), and neutrophil dysfunction. Skoutelis et al [57] found a higher rate of catheter-related infections in AIDS patients compared with oncology patients. A high prevalence of catheter-related infections due to grampositive organisms has been demonstrated in AIDS patients. Immune function at the time of CV access insertion has not been shown to predict infectious complications. Colonization of the skin, oral mucosa, and intestinal and respiratory tracts has been identified as a risk factor for systemic infections. Catheter manipulation can lead to fungal contamination of catheters, resulting in fungemia due to impaired clearance of fungal elements. Fungemia can also occur during antifungal therapy for oral or esophageal candidiasis, which affects 70% to 100% of AIDS patients. Empiric broad-spectrum antibiotics including staphylococcus prophylaxis should be initiated until culture results become available [57].

Oncology Patient. Chemotherapy and radiotherapy can cause neutropenia and thrombocytopenia. Over 60% of catheter-related sepsis occurs during periods of neutropenia (absolute count of $<500/mm^3$). Bone marrow transplant recipients are particularly susceptible to fungal and nosocomial bacterial infections during and after "conditioning" therapy. The neutropenia can last from 4 to 58 days until engraftment. In profound neutropenia (absolute count $< 200/mm^3$), the patient remains susceptible to these infections until after a successful engraftment has occurred. After engraftment, infections may be related to immunosuppressant therapy or graft-versus-host disease. Although fever is the most common

sign of infection, immunosuppressed patients may demonstrate little other evidence of infection. Empiric antibiotics should be commenced while waiting for cultures. In cases where the mechanism for neutropenia and thrombocytopenia is neoplastic bone marrow replacement (eg, hematologic malignancies) and depending on the organism isolated, infection may be managed without removal of the catheter. Riikonen et al [58] demonstrated that catheter salvage was possible in 78% of hematologic-oncologic pediatric population who were septicemic and neutropenic. In a prospective study of 966 CV access devices (93.4% subcutaneous venous ports) implanted in 933 cancer patients (70.4% solid tumors) in which patients were followed until device removal, death, or transfer of care to another facility, surgical re-intervention, neutropenia at implantation, in-hospital implantation, cuffed CV access device use, and implantation for a purpose other than chemotherapy were statistically significant risk factors for device-related bloodstream infection and pocket infection. A multidisciplinary group responsible for CV access device care and the creation of a CV access device management protocol enabled them to reduce their catheter-related infection rates from 2.2 to 0.24 per 1,000 catheter days ($P < .001$) during the study period [59].

Four prospective studies of catheter-associated thrombosis in patients with solid tumors and hematological malignancies report rates of thromboembolic events between 37% and 66% [60-63]. Thus far, routine anticoagulant prophylaxis in patients with permanent venous access devices cannot be recommended.

PN Recipients. PN recipients are often immunocompromised or critically ill. CRBSIs are major complications of PN. Although the PN itself and, in particular, the fat emulsions are well suited to bacterial and fungal growth, the majority of PN-related infections are due to contamination of the catheter rather than the infusate. Coagulase-negative staphylococci and *Staphylococcus aureus* are the primary pathogens. PN has been associated with fungemia in the pediatric and ICU populations. Increased infection rates have been noted when a lumen used for PN is used for other purposes. If a multilumen catheter is needed, a single lumen should be used exclusively for PN [10].

Cystic Fibrosis. Sufferers of cystic fibrosis may require CV access for repeated courses of intravenous antibiotics or prolonged access for PN administration. Catheter-related septicemia has been reported in up to 10% of cystic fibrosis patients, with a relatively high percentage of infections due to atypical organisms and fungi. Diabetes mellitus, corticosteroid therapy, PN, and extended courses of broad-spectrum antibiotics contribute to catheter colonization. The choice of device depends on the duration and frequency of treatment. In the outpatient setting, implanted ports may be appropriate for patients who require chronic intermittent therapy, whereas tunneled catheters may be best for those requiring more frequent access. Antifungal prophylaxis has been recommended in those with implanted ports who have impaired glucose tolerance or are undergoing corticosteroid administration. Although ports do not seem to be at increased risk of infection in this group compared with other devices, Sola et al [64] have reported SVC syndrome and DVT in up to 13.6% of these patients. Given these findings, aspirin may be prescribed.

Variant 10: Thrombotic complications. Adult or child ≥ 13 years of age. Chest port placed via right internal jugular vein is being used for chemotherapy. The infusion nurse can infuse saline but is unable to aspirate blood from the catheter

Variant 11: Thrombotic complications. Adult or child ≥ 13 years of age. Permanent hemodialysis catheter placed via the right internal jugular vein. Poor flows are documented at hemodialysis via both lumens

Variant 12: Thrombotic complications. Adult or child ≥ 13 years of age. Arm swelling secondary to extensive thrombus surrounding a triple lumen PICC placed via left basilic vein. The catheter is being used for long-term PN and intermittent intravenous antibiotics. The catheter is functioning

Thrombotic complications of CV access manifest as catheter malfunction or symptoms of DVT. The overall incidence of asymptomatic and symptomatic catheter-related DVT has been reported to be between 27% and 66% and between 0.3% and 28.3%, respectively [65]. CVC lumen occlusion affects up to 25% of CVCs placed and may be partial or complete [66,67]. It is defined as an inability to infuse solutions into or withdraw solutions from a CV access device. Causes include drug precipitation and lipid residue, anatomical or mechanical obstructions, and thrombotic occlusion. Anatomical or mechanical obstructions may be due to catheter malposition or dislocation, catheter kinking or fracture, and increased intraluminal pressures. Thrombotic occlusion is caused by the buildup of

fibrin within and around the catheter [68]. Catheter-related thrombosis can take a number of different forms: fibrin sheath, intraluminal thrombosis, and mural thrombosis. The latter refers to thrombus extending from the catheter into the lumen of a vessel and leading to partial or total catheter occlusion with or without clinical symptoms. Complications of upper extremity venous thrombosis include pulmonary embolus (incidence range 5%-14%), DVT recurrence (2%-5%), and postphlebitic syndrome (incidence range 10%-28%) [69-75]. It is incumbent on the interventional radiologist to implement preventive measures into the CV access practice and be equipped to deal with thrombotic complications as they arise.

Preventive Measures

1. Device type and placement
   a. Use catheters made from less thrombogenic materials (eg, silicone, second- and third-generation polyurethane).
   b. Use a catheter with the least number of lumens required. The risk of thrombosis increases with the number of catheter lumens used [47].
   c. The catheter tip should be placed in the caudal SVC. Venous thrombosis is more common in catheters inserted from the left side with the tip in the subclavian or innominate veins compared with tip placement in the SVC or right atrium [76].
   d. A greater vessel length exposed to a catheter seems to increase the risk of thrombosis. Left-sided placements are associated with higher incidence of DVT than right-sided catheters [62,77,78]. A prospective RCT in post–critical care patients observed a substantially higher risk of thrombotic complications (27.2%) in PICCS compared with short-term centrally placed CVCs (9.6%) [79]. Higher rates of symptomatic thrombosis (5.8% versus 1.7%; $P = .003$) were also reported in hemato-oncology patients who underwent PICC placement (346 patients) compared with tunneled CVC (247 patients), respectively [80].
   e. Catheters impregnated with antithrombotic substances including heparin-antithrombin III are available, but given the lack of long-term data relating to the safety and efficacy of these catheters, there is inadequate evidence to support their use in routine practice.
   f. Ultrasound-guided placement minimizes endothelial damage and reduces the risk of catheter-associated thrombosis at the puncture site. Two

meta-analyses have shown a substantial reduction in mechanical complications, the number of attempts at required cannulation, and the number of failed attempts at cannulation compared with the standard landmark placement when real-time 2-D ultrasound was used for placement [81,82]. Given these findings, it is likely that ultrasound guidance also reduces the risk of catheter-related thrombosis. Ultrasound guidance by an appropriately trained operator is now recommended for all nonemergent CV-access procedures by several scientific bodies [83-86].

2. Catheter flushing

Flushing of the catheter ports is routinely performed to maintain patency, reducing fibrin sheath, and clot formation [87]. Because thrombosis is a major risk factor for CVC infection, catheter flushing is also performed to reduce the risk of CRBSI. The ideal flush solution, concentration, and the flushing interval have not been defined.

   a. Saline and unfractionated heparin are equally effective to prevent thrombotic complications. Heparin at doses of 500 to 5,000 units has been the most commonly used agent. Although long-term CVCs are usually flushed at least once a month, a recent retrospective study showed that CVCs flushed less frequently were not associated with an increased rate of catheter complications [88].
   b. Recombinant tissue plasminogen activator (rTPA) (1 mg in each lumen) applied weekly as a locking solution lowered the risk of catheter dysfunction and infection in hemodialysis patients [89]. A decrease in the number of catheter-related infections has been reported with the use of rTPA in patients with hemophilia [90].
   c. Urokinase has similar efficacy as a locking solution for CVCs.
   d. Gentamicin-citrate solution was compared with heparin in a prospective multicenter study involving 555 patients with tunneled hemodialysis catheters. CRBSI in the antibiotic lock period (0.45 per 1,000 catheter-days) was 73% less than that for the heparin period (1.68 per 1,000 catheter-days) ($P = .001$). The antibiotic lock solution was the first to demonstrate a reduction in mortality in this patient population [91]. A systematic review and meta-analysis of 13 RCTs comparing sodium citrate versus heparin in hemodialysis patients showed antimicrobial-containing citrate locks (citrate + gentamicin, citrate + taurolidine, citrate + methylene blue +

methylparaben + propylparaben) to be superior in the prevention of CRBSI ($P < .001$, $P = .003$, $P = .008$, respectively). Citrate alone was less effective. The incidence of bleeding episodes was significantly lower in patients receiving citrate locks. Exit site infections, catheter removal for poor flow, thrombolytic treatment, all-cause death, catheter thrombosis, mean catheter duration, CRBSI-free catheter survival, and catheter-related readmission were similar among the two groups [92].

3. Low-dose systemic prophylactic anticoagulation and thrombolytics

There is inadequate evidence to support the routine use of low molecular weight heparin (LMWH), low-dose vitamin K antagonists (warfarin 1 mg daily), or vitamin K antagonists to maintain an international normalized ratio between 1.5 and 2, continuous intravenous unfractionated heparin, or fibrinolytics to prevent symptomatic catheter-related thrombosis in comparison with no prophylaxis [93-96].

Management of Catheter Occlusion

1. Rule out mechanical problems
   a. Attempt to aspirate blood with the patient in a supine, sitting, or standing position, with the ipsilateral arm raised.
   b. Radiograph to exclude an internal kink, fracture, or dislocation of the catheter.
2. Chemical intervention

Precipitation of drugs with low or high pH or parenteral infusions with lipid-rich emulsions may be treated with sodium bicarbonate, hydrochloric acid, and ethanol, respectively. A volume equal to the catheter fill volume should be instilled for up to 20 min.

3. Thrombotic occlusion

Contrast study of the catheter should be performed if a thrombotic complication is suspected. Drug interventions for intraluminal thrombus or thrombus at the catheter tip include:
   a. Partial occlusion: Unfractionated heparin 5,000 to 25,000 units over 6 to 24 hours [97].
   b. Complete occlusion: 1 to 2 doses of urokinase or rTPA may be administered. In one study using rTPA (2 mg/2 mL), function was reported within 2 hours in 90% of cases [98]. Similar results for rTPA were later confirmed in a large RCT including over 1,000 patients [99]. Where thrombolysis is the indication for use, 1 mg rTPA is equivalent to 36,000 units of urokinase.

4. Management of fibrin sheath

Fibrin sheath formation is seen in up to 76% of short- or long-term CVC by pull-back venography [100]. The sheath can form as early as 24 hours after catheter insertion and encase its entire length within 5 to 7 days. Mechanical treatment options for dealing with a fibrin sheath include catheter exchange, disruption using a wire or angioplasty balloon, and fibrin sheath stripping. Such interventions are indicated when pharmacologic therapy fails to restore catheter tip patency. A retrospective review of 66 procedures performed in patients with poor flow through tunneled hemodialysis catheters, despite rTPA administration, showed similar cumulative catheter patency rates at 1 month, 3 months, and 6 months among the three groups: catheter exchange, fibrin sheath stripping, and fibrin sheath disruption. The results were similar to those reported elsewhere for fibrin sheath stripping and catheter exchange: cumulative patency rates of 31% to 93% at 1 month and 45% to 56% at 3 months [101].

Management of Catheter-Related DVT

1. Anticoagulation

There is insufficient evidence in cancer patients to support the routine use of LMWH and a vitamin K antagonist or long-term LMWH for the treatment of CVC-related thrombosis. Based on good evidence supporting the use of LMWH in lower limb DVT or pulmonary embolism in cancer patients, the International Society on Thrombosis and Hemostasis recommend the use of LMWH alone for a minimum of 3 months for the treatment of catheter-related thrombosis, depending on the clinical status of the patient [102]. To date, there have been no published data regarding the use of newer anticoagulants, such as fondaparinux, dabigatran, or rivaroxaban in the treatment of patients with upper extremity or catheter-related DVT.

2. Catheter removal

A catheter that is no longer required should be removed. If the catheter is functioning and CV access is needed, then the device should be left in place and anticoagulation commenced. If the risk of pulmonary embolus is high, the catheter should be removed several days after commencing anticoagulation therapy, otherwise the catheter can be removed immediately. The patient should remain on anticoagulation for at least 3 months or as long as the CVC remains in place.

3. Catheter or systemic thrombolysis

In patients with upper extremity DVT, these therapeutic strategies have been studied only in small, retrospective case series [103,104]. In the largest retrospective cohort study of systemic thrombolysis in upper extremity DVT, the rates of DVT recurrence were similar between patients treated with thrombolysis or standard anticoagulation. However, systemic thrombolysis significantly increases the risk for major bleeding (15% versus 0%) [105]. Catheter-directed thrombolysis may be safer, but data are limited [104]. A thrombolytic or surgical approach is often considered in patients with extensive or massive thrombosis, but there is no evidence that such a strategy is superior over anticoagulant therapy alone in reducing the risk of recurrent thrombosis, pulmonary embolism, or postthrombotic syndrome in patients with upper extremity DVT [97].

4. SVC filter placement

SVC filter placement should be limited to patients with a contraindication to anticoagulation therapy and to those with thrombus progression of symptomatic pulmonary embolism despite adequate treatment with anticoagulants. Placement of a SVC filter is technically more difficult than an inferior vena cava filter because of the shorter length of the SVC. In a review that included 209 patients treated with SVC filters, 3.8% had severe complications, including cardiac tamponade, aortic perforation, and recurrent pneumothorax [106]. Although mortality rates reported after filter placement are high, mortality is almost always related to the underlying disease [107,108].

Variant 13: Infectious complications. Adult or child ≥ 13 years of age. Preventive measures to reduce catheter-related bloodstream infections when placing a nontunneled central venous catheter in ICU patient

Variant 14: Infectious complications. Adult or child ≥ 13 years of age. Therapeutic measures to manage catheter-related bloodstream infections

A CRBSI is defined as at least two blood cultures positive with the same organism, obtained from at least two separate sites at different times, in association with evidence of colonization of the catheter with the same organism. A central line–associated bloodstream infection is a term used by CDCs National Healthcare Safety Network. It is defined as a primary bloodstream infection in a patient that had a central line within the 48-hour period before the development of the bloodstream infection and is not related to an infection at another site. Because bloodstream infections may be due to sources other than a central line, this definition may overestimate the true incidence of CRBSI. A tunnel infection is characterized by pain and induration along the track of the catheter. An insertion site infection (ISI) is characterized by erythema, tenderness, and occasionally a discharge.

Infectious complications of CVCs present a significant health care burden and impose a great cost to hospitals for their management. In the United States, approximately 80,000 cases of CRBSI occur in ICUs each year. Every new episode of CRBSI increases the risk of death, in addition to prolonging ICU stay [109-111]. Management of CRBSI requires a multidisciplinary approach. As such, recommendations from diverse fields such as infectious disease, critical care, and interventional radiology should be implemented for optimal management of CRBSI and ISI.

The primary source of catheter-related infections in acute CV access devices is the patient's own skin (65%); the second most common source is the hub of the catheter (30%), and other pathways (5%) [112]. In long-term catheters, the primary source is the hub. The most commonly identified organisms in catheter-related infections are coagulase-negative staphylococcus, *S aureus*, Candida species, enteric gram-negative bacilli, and *Pseudomonas aeruginosa* [111,113]. Broadly speaking, the management of CRBSI and ISIs can be divided into prophylaxis and prevention, and therapeutic intervention. In 2011, the CDC and Healthcare Infection Control Practices Advisory Committee published evidence-based guidelines for the prevention of intravascular catheter-related infections [24].

Prevention

1. Predisposing factors

Factors predisposing to CRBSI include length of ICU stay before catheter insertion, insertion in the jugular or femoral vein, and utilization of the catheter to deliver PN [114]. Conversely, the use of a CVC to deliver antibiotics decreased the risk of CRBSI [115]. Additionally, duration of device retention has been shown to increase the risk of CRBSI. It was found that the use of a chest port for more than 33 days and a nontunneled CVC for more than 10 days carried an increased risk of CRBSI [116]. Chest ports carried a bloodstream infection rate of 2.81 cases per 1,000 days of use and nontunneled central lines carried a bloodstream infection rate of 5.60 cases of bloodstream infection per 1,000 days of use

[116]. Gunst et al [117] found that the only predictor of CRBSI infection was the duration the line was in place. Of the lines studied, infected and noninfected CVCs were in place a mean of 25 and 16 days, respectively. The single infected PICC was in place for 19 days, whereas the remaining catheters were in place a mean of 14 days. Other factors that may impact the rate of CRBSI include heavy microbial colonization at the insertion site or the catheter hub and neutropenia.

2. Education and training

Those responsible for the placement of CV access must ensure that health care personnel are educated and trained regarding the indications for intravascular catheter use, proper procedures for the insertion and maintenance of intravascular catheters, and appropriate infection control measures to prevent intravascular catheter-related infections. Knowledge of and adherence to guidelines by all personnel involved in the CV access service should be evaluated periodically [24].

3. Insertion technique and maintenance

The compilation of recommendations for placement technique is a multimodal undertaking spanning nurses, physicians, and other providers. Numerous studies and guidelines are in concordance regarding sterile technique and barrier precautions during placement. Little controversy exists regarding this issue. The 2011 CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections include step-by-step, evidence-based recommendations relating to the prevention of catheter-related infection when inserting and maintaining these devices [24].

   a. Hand-hygiene procedures, including washing hands with conventional soap and water or alcohol-based hand rubs, should be performed before and after all catheter-related interventions and palpation of the catheter insertion site. Sterile gloves should be worn when inserting CVCs, when exchanging catheters over a guide wire, and for dressing changes.

   b. Maximum sterile barrier precautions including cap, mask, sterile gown, sterile gloves, and a sterile full-body drape should be used for insertion of CVCs, PICCs, or guide-wire exchange.

   c. Antiseptic skin preparation before CVC insertion and during dressing changes should be performed with >0.5% chlorhexidine preparation with alcohol.

   d. Catheter skin site should be covered with either sterile gauze or sterile transparent semipermeable dressing. For short-term CVC sites, dressings should be changed every second day for gauze dressings and weekly for transparent dressings. Transparent dressings on tunneled or implanted CVC sites should be changed weekly until the insertion site has healed. There are no recommendations relating to the need for a dressing on well-healed exit sites of long-term cuffed and tunneled CVCs. Chlorhexidine-impregnated sponge dressings are only recommended for temporary short-term catheters if the central line–associated bloodstream infection rate persists despite adherence to routine preventive measures. Patients should be encouraged to monitor the catheter skin sites and report any new symptoms suggestive of a local or bloodstream infection.

   e. Daily skin cleansing with a 2% chlorhexidine-impregnated wash cloth is aimed at reducing the incidence of multidrug-resistant CRBSI in those with short-term catheters. In a study of 836 ICU patients, Bleasdale et al [118] reported a significant reduction in the risk of bloodstream infections among patients cleansed with chlorhexidine wash compared with soap and water (4.1 versus 10.4 infections per 1,000 patient days, 95% confidence interval 1.2-11.0). In a prospective single arm study involving 1,787 medical ICU patients bathed with soap and water baths, chlorhexidine-saturated cloth baths, or nonmedicated cloth baths, the risk of vancomycin-resistant enterococcus colonization on patient's skin was $2.5\log_{10}$ less for those cleansed with the chlorhexidine mix [119]. The incidence of vancomycin-resistant enterococcus acquisition decreased from 26 colonizations per 1,000 patient-days to 9 per 1,000 patient-days (risk ratio, 0.4; 95% confidence interval 0.1-0.9). The relative risk of vancomycin-resistant enterococcus contamination of health care workers' hands was 0.6 (95% confidence interval 0.4-0.8) and of environmental surfaces was 0.3 (95% confidence interval 0.2-0.5). More recently, further support for chlorhexidine baths came from a multicenter cluster-randomized non-blinded crossover trial in which the acquisition of multidrug-resistant organisms and the incidence of hospital-acquired bloodstream infections were compared in patients cleansed with chlorhexidine-impregnated washcloths or nonantimicrobial

washcloths. A total of 7,727 study patients were enrolled over a 1- to 2-month period. The overall rate of multidrug-resistant organism acquisition was 5.10 cases per 1,000 patient-days with chlorhexidine bathing versus 6.60 cases per 1,000 patient-days with non-antimicrobial washcloths (P = .03) (23% lower with chlorhexidine bathing). The overall rate of hospital-acquired bloodstream infections was 4.78 cases per 1,000 patient-days with chlorhexidine bathing versus 6.60 cases per 1,000 patient-days with nonantimicrobial washcloths (P = .007), (28% lower with chlorhexidine-impregnated washcloths). Although the study supported earlier findings of a significant reduction in gram-positive bacteremias, it also demonstrated a lower rate of CVC-related fungemia.

   f. Other targeted interventions that may reduce CVC-related infections include the use of a sutureless securement device [120], the use of a needleless infusion system [121-123], disinfection of the needleless connector devices with chlorhexidine or alcohol solutions [121,124], and the use of antiseptic barrier caps for needleless connectors [125,126].

4. Site selection

Although there remains some discussion regarding subclavian versus internal jugular placement of CVCs, there is general consensus that selection of an upper body insertion site should be considered to minimize the risk of infection in adult patients [40,46,47]. Although one study found that insertion of nontunneled CVCs in the jugular or femoral vein prolonged ICU stay compared with subclavian vein access, this must be weighed against certain increased risks associated with subclavian line insertion such as pneumothorax. Catheters should be placed as far away as possible from open wounds. A multicenter trial in which the placement of nontunneled CVCs in 3,027 ICU patients were randomly assigned to the subclavian, jugular, or femoral veins reported lower risk of bloodstream infection and symptomatic thrombosis but higher rates of pneumothorax among patients who underwent subclavian vein catheterization compared with those who underwent jugular vein or femoral vein catheterization [50]. This finding supports the CDC 2011 recommendation to place nontunneled CVC in adult patients at a subclavian site rather than jugular or femoral venous sites to minimize infection risk [127]. No recommendation can be made for a preferred site of insertion to minimize infection risk for a tunneled CVC.

5. Device selection

The daily infection rate with CVCs is about 20 times higher than with peripheral catheters. The most serious CRBSIs occur in the setting of short-term nontunneled catheters placed via central vein [7]. The infection rate increases exponentially over time with their use. Rates of bacteremia are extremely high in nontunneled catheters within 2 to 4 weeks after placement [105]. In general, a lower rate of infection is documented with totally implantable devices [7]. Long-term catheters that are tunneled (eg, Hickman, Broviac, or Groshong catheters, C. R. Bard, Inc, Salt Lake City UT) seem to have one-quarter of the daily risk associated with nontunneled central lines, but still pose a much higher risk than peripheral catheters. In one study, implanted ports had the lowest incidence of CRBSI (0.1 per 1,000 catheter days). In this same study, the incidence of CRBSI among tunneled and nontunneled CVCs were 1.6 per 1,000 catheter days and 2.7 per 1,000 catheter days, respectively [105]. Teichgraber et al [6] found that CRBSI related to ports was only 5.1% at 0.15 per 1,000 catheter days.

There is no consensus regarding infectious complications of PICCs. Leonidou et al [7] found that PICCs seem to have a similar risk of infection to central lines in ICUs. In another study, PICCs were associated with fewer CRBSIs in long-term surgical ICU patients (allowing for the fact that CVCs were in place somewhat longer than PICCs) [117]. In this study, there were 263 CVCs and 37 PICCs placed. Of the CVCs, 4.9% became infected, an infection rate of 6.0 per 1,000 catheter-days. Of the 37 PICCs placed, 2.7% became infected, a rate of 2.2 infections per 1,000 catheter-days [117].

The use of catheters for hemodialysis is the most common factor contributing to bacteremia in dialysis patients [128,129]. The relative risk for bacteremia in patients with dialysis catheters is 7-fold the risk for patients with arteriovenous fistula [130]. If temporary access is needed for dialysis, a tunneled cuffed catheter is preferable to a noncuffed catheter, even in the ICU setting, if the catheter is expected to stay in place for >3 weeks [31].

Polytetrafluoroethylene (Teflon, The Chemours Company, Wilmington, Delaware, USA) or polyurethane catheters have been associated with fewer infectious complications than catheters made of polyvinyl chloride or polyethylene [11,12]. The use of anti-infective

agents (aside from antibiotics) in conjunction with CVCs has been shown to reduce the rates of CRBSI for durations of between 5 and 12 days and greater than 20 days when CVCs are inserted in the femoral or jugular veins. Studies report the best clinical effect when CVCs are treated with a combination of minocycline and rifampin or internally and externally treated with silver or chlorhexidine and silver sulfadiazine [16-21,23]. Current evidence suggests that anti-infectives are cost-effective for high-risk patients compared with standard CVCs. Additional anti-infective agents demonstrated to have variable levels of efficacy include carbon and platinum, cuffs impregnated with silver, and benzalkonium chloride [131].

Catheter-related thrombosis is closely linked to CRBSI. Thrombus can serve as a nidus for infection. To this end, Wang et al [132] analyzed 45 trials with 12,085 enrolled CVCs. It was found that adjusted heparin-bonded catheters and minocycline and rifampicin catheters were associated with a significantly lower rate of CRBSI than standard catheters. It was concluded that rifampicin-based impregnated catheters were better for prevention of catheter-related infection compared with the other catheters. Wang et al also found that for prevention of CVC colonization, adjusted silver iontophoretic catheters, chlorhexidine and silver sulfadiazine catheters, chlorhexidine and silver sulfadiazine blue plus catheters, minocycline and rifampicin catheters, and miconazole and rifampicin catheters were associated with a significantly lower rate of catheter colonization compared with standard catheters. The ultimate conclusion of this large scale meta-analysis was that rifampicin-based impregnated CVC was the only type of CVC that reduced both catheter colonization and CRBSI compared with standard CVCs and that rifampicin-based impregnated catheters seem to be more effective for prevention of catheter-related infection [132].

Other impregnated compounds have also been investigated. In critically ill patients, the use of silver-nanoparticle-impregnated CVCs had no significant effect on CVC colonization, CRBSI incidence, or ICU mortality [133].

6. Prophylactic antibiotics

Use of prophylactic antibiotics before CV access placement remains controversial and poorly studied. In one study that examined the use of prophylactic antibiotics in 404 patients before chest port placement, Karanlik et al [134] found that 1 g of cefazolin given preprocedure had no significant impact on the already low rate of postoperative infectious complications (overall rate of surgical site infection was 2.7%). No difference in the incidence of infectious complications was found in either group. Covey et al [135] reached a similar conclusion in that the rate of early infection without antibiotic prophylaxis before chest port placement in the interventional radiology suite was only 1%. Based on their data, use of prophylactic antibiotics for implanted devices was not recommended. Additionally, there was no significant difference between the rates of device removal because of infections in patients who received antibiotics before the procedure versus patients who did not receive antibiotics. The CDC recommends against the routine administration of systemic antimicrobial prophylaxis before insertion or during use of an intravascular catheter to prevent catheter colonization or CRBSI [136]. In nononcology patients, no benefit was associated with vancomycin administration before catheter insertion in 55 patients undergoing catheterization for PN [137]. Extending perioperative prophylactic antibiotics in cardiovascular surgery patients did not reduce CVC colonization [115]. For immunocompromised patients, administration of intravenous antibiotic prophylaxis should be considered on a case-by-case basis.

7. Topical applications

Several antibiotic and anti-infective agents have been tested at the surgical insertion site in an attempt to reduce catheter-related infection. In three RCTS involving hemodialysis patients, the use of 10% povidone iodine was associated with a significant decrease in colonization, exit-site infection, or bloodstream infection. The beneficial effect was most prominent in subjects with nasal colonization by *S aureus* [138-140]. Mupirocin ointment applied either at the catheter insertion site or nasally has been shown to reduce the risk of CRBSI; however, this has been offset by an increase in mupirocin resistance in some centers and the potential for the drug to degrade polyurethane catheters.

8. Catheter locking solutions (covered under Thrombotic complications)

Management

1. Diagnosis of CRBSI

Numerous studies and guidelines exist in the critical care and infectious disease literature regarding the

methodology of diagnosing CRBSI. This is an important issue, because it was found in one study that more than 70% of the suspected CRBSIs yielded negative blood culture results (no growth), meaning that the catheter was unnecessarily removed [141]. In that same study, there was no statistically significant difference between the standard and conservative methods of diagnosing CRBSI, with regards to in-hospital mortality. The standard method consisted of culturing the catheter tip, plus a culture of a peripheral blood sample. A differential time to positivity of 2 hours (cutoff limit) is a very sensitive and specific predictor of catheter-related bacteremia [142,143]. The conservative method consisted of obtaining peripheral and catheter blood samples at different times with analysis of the number of colonies. Of the 29 deaths occurring in the ICU, 17 (58.6%) were from the conservative method group and 12 (41.3%) were from the standard method group. The study showed no difference in mortality rates of patients with CRBSI when the two methods of diagnosis were compared. However, there was noted to be a difference in mortality when the standard method was compared with the conservative method in cases where the catheter is kept in place for more than 24 hours (56% versus 100%) [141]. Nakazawa et al [144] reported a much higher rate of false-positives with blood cultures obtained from catheters compared with peripheral sites due to catheter hub contamination.

In relation to the hematology and oncology patient population, certain aspects of diagnosing CRBSI are similar to those of the general population [145]. At least two of the following three symptoms are required to diagnose local infection: redness, induration, or tenderness within 2 cm of the venipuncture site. In patients with suspected or local infection without signs of systemic infection, two pairs of blood cultures should be taken—one from a peripheral vein and one from the CVC. The difference in time between positivity of results of catheter culture and peripheral blood culture has been found be an important diagnostic indicator (differential time to positivity) [145].

2. Catheter removal or retention

Convention has long dictated that after CRBSI has been demonstrated, the catheter is to be removed. However, in patients with limited access, this is often not feasible. In general, a catheter should be removed if the patient has unexplained sepsis or erythema overlying the catheter insertion site or purulence at the catheter insertion site or if the CRBSI is associated with supportive thrombophlebitis, endocarditis, or osteomyelitis [7]. Additionally, catheter removal is necessary if *S aureus* is isolated from blood cultures of a patient with an indwelling CVC. It has been shown that attempts for catheter preservation in subjects with catheter-related infection due to *S aureus* have no more than a 20% chance of success. Preservation of the catheter may be attempted in clinically stable patients, in whom coagulase-negative staphylococci, *Corynebacterium jeikeium, Acinetobacter baumannii, Stenotrophomonas maltophilia, P aeruginosa,* and bacillus species have been detected as infections. In clinically stable patients with fever of unknown origin, the catheter should not routinely be removed without microbiological evidence of catheter-related infection [141,145].

Leonidou et al [7] have stated that long-term CVC or ports should be removed from patients with CRBSI associated with any of the following conditions: severe sepsis, supportive thrombophlebitis, endocarditis, bloodstream infection that continues despite 72 hours of antimicrobial therapy to which the infecting microbes are susceptible, or diagnosis of a port abscess. Salvage therapy can be considered in uncomplicated CRBSI where patients have limited access options and long-term intravascular access is required. Both systemic and antimicrobial lock therapy should be used, repeated blood cultures obtained, and the catheter removed if blood cultures remain positive for a micro-organism when drawn 72 hours after initiation of appropriate therapy [7].

Routine replacement of CVCs, PICCs, and hemodialysis catheters to prevent infection should be avoided in adults and children. Routine guide-wire exchanges of nontunneled CVCs in an effort to prevent CRBSI should be avoided. In select patients with tunneled hemodialysis catheters and bacteremia and limited venous access, catheter exchange over a guide wire, in combination with antibiotic therapy, is an alternative as a salvage strategy [146-148].

3. Treatment recommendations

The microbes that colonize catheter hubs and the skin surrounding the insertion site are the source of most CRBSIs. The micro-organisms involved in CRBSI have been shown, via electron microscopy, to be embedded in a biofilm matrix. Additionally, the number of organisms on the catheter tip is related to the occurrence of CRBSI [7]. The micro-organisms most often isolated

from intravascular catheters are coagulase-negative staphylococci, followed by candida, *S aureus*, *enterococcus*, *pseudomonas*, and *acinetobacter* [7,116]. For infections localized to the exit site, treatment with antibiotics alone may be adequate [105].

a. Coagulase-negative staphylococci: Coagulase-negative staphylococci are the most common pathogens in CRBSIs. A diagnosis of bacteremia requires at least two positive blood cultures, including one drawn from a peripheral vein. Although catheter removal may be sufficient to resolve the infection, it is generally recommended that the patient also be treated with a week of intravenous antibiotics. If the CVC is to be retained, a longer duration of therapy consisting of 10 to 14 days, together with antibiotic lock therapy, is advised. In the 20% of cases that fail to respond to these measures (persistent fever and bacteremia), the catheter should be removed [149]. Vancomycin, systemically and as a catheter lock therapy, is frequently used in institutions with a high prevalence of methicillin-resistant *S aureus*. Where methicillin-resistant *S aureus* isolates with vancomycin inhibitory concentration values > 1 mg/mL are identified, alternative agents (eg, daptomycin) should be considered [110].

b. *S aureus*: Catheter removal is advised if a non-tunneled CVC is suspected to be the source of *S aureus* bacteremia, or in the case of a tunneled device, there is evidence of a tunnel infection or ISI [99]. A new catheter should then be placed at a different site. Uncomplicated cases should be treated with intravenous antibiotics for a minimum of 10 to 14 days after catheter removal [110]. Caution should be exercised when considering catheter salvage. Failure or a delay in catheter removal has been associated with increased risk of hematogenous complications and increased mortality. The risk of such complications should be taken into account when deciding on the duration of therapy. Antibiotic treatment depends on sensitivities and may include penicillin, a first-generation cephalosporin, vancomycin, daptomycin, or linezolid [7].

c. Enterococcus: The incidence of enterococcal infection associated with CVCs has increased substantially. The ability of the organisms to form a biofilm can make antimicrobial treatment more difficult. The Infectious Diseases Society of America (IDSA) guidelines for the treatment of enterococcal CRBSI caused by susceptible isolates advise either ampicillin or vancomycin alone or in combination with an aminoglycoside [110]. If ampicillin- and vancomycin-resistant enterococci are isolated, linezolid or daptomycin may be considered. If a long-term catheter is retained in cases of uncomplicated infection, 7 to 14 days of intravenous treatment is recommended in addition to antibiotic lock therapy [150].

d. Candida CRBSI: Candida species are the second most common cause of infection in the setting of a vascular catheter and are associated with increased mortality, extended hospital stays, and high cost [151]. Because catheter retention has been associated with poorer outcomes, catheter removal within 72 hours is advised. Of note, a study of 404 oncology patients with CVC and candidemia identified the catheter as the source of infection in only 27% [143]. With this in mind, efforts should be made to rule out other possible sources of the fungemia. The IDSA guidelines recommend antifungal therapy with fluconazole or an echinocandin for all CRBSI due to Candida species for 2 weeks after the last positive blood culture [110]. Data relating to antifungal lock therapies are lacking [7].

e. Gram-negative bacilli: Data concerning the management of CRBSI due to gram-negative bacilli are limited. Although the incidence of CRBSI due to gram-negative bacilli has decreased, multidrug resistance has become a concern. A high frequency of treatment failure and relapse has been documented if the CVC is retained [152]. The IDSA guidelines recommend empiric antibiotic therapy in septic, critically ill, or neutropenic patients; those with femoral catheter in place; and those with known focus of infection because these patients are at higher risk for infection due to multidrug-resistant gram-negative bacilli [110]. Two different-class antimicrobial agents should be commenced in critically ill patients with suspected CRBSI and recent colonization of infection with a multidrug-resistant gram-negative bacillus until cultures and drug sensitivities become available.

SUMMARY OF RECOMMENDATIONS

- A tunneled double-lumen small-bore CVC and chest port are the best choices for intravenous access for the administration of long-term total PN and

intermittent intravenous antibiotics. Chest ports are recommended as the first choice for intravenous access for the treatment of recurrent sickle cell crisis.

- A tunneled small-bore single-lumen CVC provides the best CV access option for the administration of long-term antibiotics (6 weeks or more) in patients with stage 3 chronic kidney disease. A nontunneled CVC is the most appropriate CVC to use in a patient admitted to the hospital with acute or chronic renal insufficiency requiring short-term antibiotics (approximately 7-10 days) for acute sepsis.

- The contralateral internal jugular vein is the most appropriate venous access site for hemodialysis in a patient with end-stage renal disease who has undergone creation of an arteriovenous fistula and the fistula has not yet matured.

- The presence of fever and malaise alone in an immunocompromised patient is not an indication for removal of a tunneled CVC. However, the catheter should be removed if positive blood cultures are confirmed.

- For a patient requiring head and neck surgery for cancer, arm or chest ports and PICCs are recommended for intravenous access for chemotherapy.

- Chest radiograph and contrast study of the catheter are the recommended first steps for assessing a dysfunctional chest port and other CVCs.

- For suspected thrombotic complications leading to a dysfunctional tunneled dialysis catheter, catheter removal and placement of a new catheter from a different site, catheter exchange, contrast study of the catheter, and fibrin sheath stripping or disruption are excellent next steps. An attempt should be made to perform dialysis with the patient arm in a different position. Arm swelling secondary to extensive thrombus surrounding a functioning, in-use peripherally inserted CVC should be treated by anticoagulation without removal of the catheter.

- Preventive measures to reduce the risk of CRBSI when placing a nontunneled CVC in ICU patients include upper body insertion site. The catheter should be removed in the setting of *S aureus* bacteremia. Catheter salvage and concomitant antibiotic therapy are appropriate in patients with limited venous access.

SUMMARY OF EVIDENCE

Of the 152 references cited in the ACR Appropriateness Criteria® Radiologic Management of Central Venous Access document, 133 are categorized as therapeutic references including 47 well-designed studies, 43 good-quality studies, and 2 quality studies that may have design limitations. Additionally, 5 references are categorized as diagnostic references including 1 good-quality study. There are 45 references that may not be useful as primary evidence. There are 14 references that are meta-analysis studies.

The 152 references cited in the ACR Appropriateness Criteria® Radiologic Management of Central Venous Access document were published from 1977 to 2015.

Although there are references that report on studies with design limitations, 91 well-designed or good-quality studies provide good evidence.

SUPPORTING DOCUMENTS

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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