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Intravascular Catheter-Related Bloodstream Infection

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Abstract

Intravascular catheters required for the care of many hospitalized patients can give rise to bloodstream infection, a complication of care that has occurred most frequently in intensive care unit (ICU) settings. Elucidation of the pathogenesis of catheter-related bloodstream infections (CRBSIs) has guided development of effective diagnostic, management, and prevention strategies. When CRBSIs occur in the ICU, physicians must be prepared to recognize and treat them. Prevention of these infections requires careful attention to optimal catheter selection, insertion and maintenance, and to removal of catheters when they are no longer needed. This review provides a succinct summary of the epidemiology, pathogenesis, and microbiology of CRBSIs and a review of current guidance for the diagnosis, management, and prevention of these infections.

Keywords

infectious disease medicine, clinical specialty, neurocritical care, clinical specialty, safety techniques

Introduction

In the last 60 years, venous access via catheter insertion has become a very common practice in the hospital and outpatient settings for various purposes, including hemodynamic monitoring, renal replacement therapy, nutritional support, and medication administration. In 1929, Forssmann introduced one of the first techniques for central venous catheterization and shared the 1956 Nobel Prize for Medicine along with 2 other colleagues for pioneering work in this field.[1] Since then, catheter insertion techniques and indications for placement have evolved and currently about 150 million intravascular devices are used every year in the United States.[2] Unfortunately, these catheters can introduce infection to the bloodstream. As a consequence of their increasing use, bloodstream infections resulting from intravascular catheters have become a costly complication of health care, with estimates in the United States ranging from 670 million to 2.68 billion dollars annually.[3] To reduce costs the Centers for Medicare and Medicare Services (CMS) is no longer paying for the care of hospital-associated vascular catheter infections,[4] and to promote prevention it provides a financial incentive to hospitals for public reporting of rates of central line-associated bloodstream infections occurring in their intensive care unit (ICU) patients.[5] Optimal management and prevention of these infections have become priorities of most health care facilities.

Definitions

Bloodstream infection refers to the recovery of a microbial pathogen in blood culture by virtue of infection, not specimen contamination. Catheter-related bloodstream infection (CRBSI) refers to bloodstream infection attributed to an intravascular catheter by quantitative culture of the catheter tip or by differences in growth between catheter and peripheral venipuncture blood culture specimens (see Diagnosis section). A central venous catheter is a catheter whose tip resides in a central vein, whereas the tip of peripheral venous catheter does not. (A peripherally inserted central catheter is a central venous catheter.) Central venous catheter and central line are used interchangeably. A long-term central venous catheter is a central venous catheter that is intended to remain in place for a prolonged or indefinite period of time; it is either tunneled subcutaneously between the percutaneous exit site and the site of vein entry, or it is fully implanted with a subcutaneous chamber that has a rubber surface which is accessed by a

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Table 1. Estimates of Bloodstream Infections Attributed to Vascular Catheters by Catheter Type.[7]

Catheter	Catheter-Related Bloodstream Infection	
	Incidence (%)	Incidence Density (Number/1000 Line Days)
Peripheral venous	0.1	0.5
Arterial	0.4	0.2
Peripherally inserted central catheters (PICC)	2.4	2.1
Short-term central venous catheter	4.4	2.7
Percutaneous, tunneled long-term central venous catheter	22.5	1.6
Fully implanted, tunneled long-term central venous catheter	3.6	0.1

noncoring metal (Huber) needle. A short-term central venous catheter is intended for temporary use and it is neither tunneled subcutaneously nor fully implanted. Central line-associated blood stream infection (CLABSI) refers to a bloodstream infection that appears in the presence of a central venous catheter or within 48 hours of removal of a central venous catheter and which cannot be attributed to an infection unrelated to the catheter; it is defined by the National Healthcare Safety Network (NHSN) for the purpose of surveillance of health care-associated infection.[6] Finally, and also for purposes of surveillance, a central line day is defined as one patient with one or more indwelling central venous catheters, residing in a health care facility at one point in time during a 24-hour period.

Of note, the different microbiologic criteria of the CRBSI and CLABSI definitions reflect the different purposes for which each was developed. The CRBSI was developed for use in research investigations of the risk factors and pathogenesis of bloodstream infections complicating vascular catheters in which it is critically important to establish a standardized, objective, unequivocal outcome. The CLABSI was developed for surveillance of health care-associated bloodstream infections in nonresearch settings in which standardized, objective, unequivocal outcomes are not available due to differences in the diagnostic laboratory investigations requested by different providers and therefore CLABSI was developed to serve as a surrogate measure of CRBSI. This will be discussed further (see Surveillance and Reporting section).

Epidemiology

Up until recently, over 250 000 CRBSIs occurred every year in the United States and over 80 000 of these appeared in ICUs.[7] These infections are associated with increased length of hospital stay from 10 to 20 days and increases in the cost of care from $4000 to $56 000.[7] Whether and how these infections are associated with increased risk of death remain to be determined.[8]

The incidence of CRBSIs may be expressed as a proportion, or percentage, of (first) infections that occur per catheter placed. However, as the risk of infection accumulates over time while the catheter is in place, a more precise measure of the incidence is the incidence density, or incidence rate, which is the number of (first) infections that occur over the number of days that the line is in place (ie, line days).

As the catheter is the principle risk factor for CRBSI, it is not surprising that the incidence, and incidence density, of these infections vary between catheter type. A recent review by Maki of over 200 published reports found estimates of incidence and incidence density of CRBSI to vary between 0.1% and 22.5% and between 0.1 and 2.7 per 1000 line days, respectively, by catheter type.[7] These findings are summarized in Table 1. Note that the incidences of infection of long-term central venous catheters are relatively high as they often remain in place until removal is required because of infection. On the other hand, the incidence densities of these infections are lower and significantly lower for ports, indicating a reduced incidence over time while the catheter remains in place.

Risk Factors

Risk factors for CRBSI include patient-, catheter-, and operator-related factors. Patient-related factors that increase risk of bloodstream infection include increasing severity of illness, granulocytopenia, compromised integrity of the skin, and presence of distant infection. Catheter type influences risk of bloodstream infection as discussed above, while risk of bloodstream infection increases for each catheter type with increasing lumen number. Antiseptic or antimicrobial coating of catheters can reduce risk of CRBSI. For nontunneled catheters, risk of bloodstream infection varies by anatomic site of insertion such that risk is greatest for groin insertion, intermediate for neck insertion, and lowest for chest or upper extremity insertion. Risk of CRBSI increases after breaks in aseptic technique during placement and maintenance and with increases in the frequency of catheter access.[8,9]

Pathogenesis

All percutaneous catheters are associated with risk of (skin) exit site infection and subsequent migration of that infection along the extraluminal catheter surface to the bloodstream.[9,10] This risk is reduced either by tunneling the catheter subcutaneously and extending the distance between the catheter–skin interface and the catheter–vessel interface, or by fully implanting the catheter. Bacterial or fungal contamination of a catheter hub can also lead to intraluminal infection of the catheter and extension of that infection to the bloodstream.[9,11]

It was once thought that hub contamination resulting in intraluminal catheter and subsequent bloodstream infection occurred exclusively in long-term central venous catheters. More recently, hub colonization and intraluminal migration

of infection has been recognized to be a common cause of both short- and long-term central venous catheters.[12] Unusual causes of CRBSI are intrinsic contamination of infusates and hematogenous seeding from distant infection.[9]

Microbiology

The leading causes of CRBSI in descending order of frequency are staphylococci (both *Staphylococcus aureus* and the coagulase-negative staphylococci), enterococci, aerobic Gram-negative bacilli and yeast. When aerobic Gram-negative bacilli are assessed as a group, their frequency follows that of the staphylococci.[9]

Certain pathogens are associated with specific host, treatment, and catheter characteristics. *S aureus* infections are disproportionately represented in infections of hemodialysis catheters.[13] Gram-negative bacilli have been associated with infections of patients with cancer, and they are typically the pathogens recovered in instances of infusate contaminations.[9,14,15] Gram-negative bacilli and yeast have been affiliated with catheters placed in femoral veins,[16] while candida have been associated with infections of lines used for administration of parenteral nutrition.[17,18]

Diagnosis

Catheter-related bloodstream infection should be suspected in a patient with an intravascular catheter who develops the clinical or laboratory criteria of the systemic inflammatory response syndrome (ie, temperature <36°C or >38°C, heart rate >90/minute, respiratory rate >20/minute, or peripheral white blood cell count <4000/μL or >12 000/μL). Exit sites of all percutaneous vascular devices should be assessed to identify obvious inflammation. If a patient with an intravascular catheter develops evidence of a systemic inflammatory response without an obvious, nonvascular site of infection, removal of the catheter should be considered and diagnostic evaluation of possible CRBSI should be undertaken.

Quantitative culture of the distal (5 cm) tip of central venous and arterial catheters should be performed when they are removed for suspected infection. The tip of the introducer should be sent for culture when a pulmonary artery line is removed. For patients with short-term central venous catheters without severe sepsis or shock, in whom the index of suspicion for catheter-related infection is moderate or less, the catheter may be exchanged over a guide wire for a new catheter allowing culture of the tip of the removed catheter without immediately sacrificing the site of insertion.[2]

At least 2 blood cultures should be obtained when catheter infection is suspected. When the tip of a catheter is sent for culture, the 2 blood cultures may be obtained by peripheral venipuncture. Alternatively or when culture of the tip of the catheter is not performed, 1 blood culture should be obtained by peripheral venipuncture and at least 1 blood culture should be obtained from a lumen of the catheter. A recent study has found that for multilumen catheters, drawing multiple catheter blood cultures, one from each lumen of the catheter suspected of infection, in addition to 1 blood culture obtained by peripheral venipuncture will enhance detection of catheter infection.[19] For patients with multiple central venous and/or arterial catheters, a blood culture should be drawn through each catheter in addition to that obtained by peripheral venipuncture; in these circumstances drawing blood cultures from all lumens of all catheters is not endorsed. To reduce the incidence of blood culture contamination, the skin and the hub of the catheter must be cleansed with alcohol, tincture of iodine or alcohol chlorhexidene, and allowed to dry, before specimen collection.[2]

Currently, most hospital microbiology laboratories use automated systems for detecting growth in incubating blood cultures. And nearly all of these will provide the time of incubation when a culture yields growth. Time of incubation, otherwise referred to as time to detection of growth or time to positivity, has been demonstrated to be a reliable surrogate measure of the microbial load in the specimen of blood obtained for culture. A few hospitals use blood culture systems (eg, lysis centrifugation) that quantify the colonies of growth recovered in each blood culture specimen.

A diagnosis of CRBSI is achieved by any of the following 3 criteria:

- same organism recovered from percutaneous blood culture and from quantitative (>15 colony-forming units) culture of the catheter tip;
- same organism recovered from a percutaneous and a catheter lumen blood culture, with growth detected 2 hours sooner (ie, 2 hours less incubation) in the latter;
- same organism recovered from a quantitative percutaneous and a catheter lumen blood culture, with 3-fold greater colony count in the latter [2]

Management: General

While awaiting the results of cultures, the following antimicrobials are recommended for empiric treatment of suspected CRBSI:

- vancomycin in institutions where the prevalence of methicillin resistance in staphylococci is increased (otherwise use a first-generation cephalosporin such as cefazolin or an anti-staphylococcal penicillin such as nafcillin);
- daptomycin in lieu of vancomycin in facilities where the prevalence of methicillin-resistant *S aureus* with reduced vancomycin susceptibility (minimum inhibitory concentration >2 mcg/mL) is increased
- antibiotics active against Gram-negative bacilli, based upon local susceptibility patterns, in the setting of increased severity of illness or femoral catheterization;

- antibiotics active against *Pseudomonas aeruginosa*, based upon local susceptibility patterns, in the setting of neutropenia, severe illness, or known colonization;
- antimicrobials active against candida, preferably an echinocandin, in the setting of femoral catheterization, total parenteral nutrition, prolonged administration of broad-spectrum antibiotics, hematologic malignancy, or solid organ or hematopoietic stem cell transplantation.[2]

If blood cultures fail to yield growth, the need for further empiric antibiotic therapy should be reassessed. If unexplained fever or sepsis persists in a patient with a short-term central venous or arterial catheter and paired peripheral venipuncture and catheter blood cultures have failed to identify CRBSI as described above, the catheter should be removed and its tip should be sent for culture.[2]

Management: Short-Term Central Venous or Arterial CRBSI

For patients in whom cultures confirm CRBSI, empiric antibiotic therapy should be adjusted to optimally address the susceptibility profile of the recovered pathogen. Review of published guidance (eg, Table 5 of reference 2) or consultation with a local infectious disease expert is advisable. Blood cultures should be repeated on therapeutic antimicrobials, and the duration of therapy, as advised below, should begin with the first day of documented absence of growth in blood culture. For patients with short-term central venous or arterial CRBSI, the infected catheter, or the catheter placed over a guide wire in exchange for the infected catheter, should be removed expeditiously. For uncomplicated bloodstream infection (ie, no associated supportive thrombosis, endocarditis, or metastatic infection) that arises in the absence of factors that increase the risk of hematogenous spread of infection (eg, no intravascular hardware, immunosupression) and which resolves within 72 hours of catheter removal, systemic therapeutic, intravenous antibiotic treatment is recommended for:

- 5 to 7 days for coagulase-negative staphylococci;
- 7 to 14 days for enterococci and Gram-negative bacilli;
- 14 days in the absence of evidence fungal retinitis for *Candida* species; and
- 14 days in the absence of evidence of endocarditis clinically and by transesophageal echocardiography (TEE), for *S aureus*.

For patients with susceptible pathogens and a functioning gastrointestinal tract, orally administered linezolid, fluoroquinolones, or fluconazole may be considered for treatment of methicillin-resistant staphylococci, Gram-negative bacilli, and candida, retrospectively. Repeat blood cultures following completion of antibiotic therapy are not recommended in the absence of clinical indication (eg, recurrent fever). For patients with short-term central venous or arterial CRBSI lasting over 72 hours, or with factors that increase the risk of metastatic infection, longer duration of antibiotic administration directed by patient, pathogen, and disease characteristics will be required. Expert opinion in the form of infectious diseases consultation should be considered to assist the evaluation and management of these more complicated infections.[2]

Management: Long-Term Central Venous CRBSI

For patients with long-term CRBSI associated with septic thrombosis, endocarditis, metastatic infection (eg, osteomyelitis), subcutaneous catheter tunnel track or port infection, the catheter should be removed immediately. Catheter removal is also recommended for *S aureus*, *Bacillus* species, micrococcus, propionibacterium, *P aeruginosa*, candida, or mycobacterial infection.[2] When cultures confirm long-term central venous catheter-associated bloodstream infection, empiric antibiotic therapy should be adjusted to optimally address the susceptibility profile of the recovered pathogen as discussed for short-term central venous CRBSI. Following removal of a long-term central venous catheter for any of the indications above, the duration of antibiotic treatment will depend upon patient, pathogen, and disease characteristics and may best be determined in consultation with an infectious disease expert. For those patients in whom the onset of catheter-related infection was indolent or subacute, the possibility of long-standing bloodstream infection and metastatic spread (eg, endovascular, intervertebral disk, prosthetic joint, etc) of infection must be considered. Four to six weeks of therapy is often required for *S aureus* infection, the specific duration again depending upon patient, pathogen, and disease characteristics. Fourteen days of administration can be considered for nondiabetic, nonneutropenic, nonimmunosuppressed patients without septic thrombosis, endocarditis (TEE negative), metastatic infection, or prosthetic intravascular devices when *S aureus* or other bacterial infection resolves within 72 hours of antibiotic initiation and catheter removal. For patients with candida infection in whom there is no suspicion or evidence of metastatic infection (including candida retinitis) and for whom fungemia and evidence of infection resolve promptly upon catheter removal, antifungal therapy should be continued for 14 days after the first negative blood culture. For patients with susceptible pathogens and a functioning gastrointestinal tract, orally administered linezolid, flouroquinolones, or fluconazole may be used to complete treatment of methicillin-resistant staphylococcal, Gram-negative bacilli, or candida infection, respectively. In general, a new long-term central venous catheter can be placed at a new anatomic site after 72 hours of effective antibiotic administration and lack of growth in repeat blood cultures.[2]

For patients with long-term central venous CRBSI unassociated with septic thrombosis, endocarditis, metastatic infection, tunnel track, or port infection caused by

Table 2. Recommended Practices for Prevention of Central Venous Catheter-Related Bloodstream Infection.[8]

- Limit insertion to trained personnel
- Avoid use of the femoral vein
- Use subclavian vein in lieu of the internal jugular or femoral vein depending upon risk of injury during insertion
- Use a central venous catheter with the minimum number of lumens required for patient care
- Complete hand hygiene prior to insertion and assessment or dressing change of catheter exit site
- Prepare clean skin of insertion site with >0.5% chlorhexidine plus alcohol
- Do not administer systemic antimicrobial prophylaxis
- Use a chlorhexidene/silver sulfadiazine or a minocycline-/rifampin-impregnated central venous catheters when the local rate of central line-associated bloodstream infection is not declining despite
    - Education of optimal insertion and maintenance practices
    - Use of maximum sterile barrier precautions during insertion
    - Use of >0.5% chlorhexidene plus alcohol for preparation of skin before insertion
- Use maximum sterile barrier precautions, including cap, mask, sterile gown, sterile gloves, and a sterile full-body drape for insertion and during guide wire exchange
    - Don new sterile gloves before inserting new catheter during exchange over guide wire
- Place semipermeable transparent or gauze dressing over insertion site
    - Gauze favored when exit site is bloody or moist
    - Restrict application of antimicrobial ointment to exit sites of hemodialysis catheters and only then when approved for use by catheter manufacturer
    - Assess exit site daily
        - Visually for transparent dressings
        - By palpation for gauze dressings (remove for visual inspection if tender)
    - Exchange exit site dressing whenever damp, loosened, or soiled
        - Replace gauze dressings every 2 days
        - Replace semipermeable transparent dressings every 7 days
- When adherence to aseptic technique was compromised during insertion, replace the catheter as soon as possible
- Do not routinely replace central venous catheters to prevent infection
- Remove any intravascular catheter as soon as it is no longer required for patient care

Table 3. Recommended Practices for Prevention of Arterial Catheter-Related Bloodstream Infection.[8]

- Selection of radial, brachial, or dorsalis pedis sites for insertion in lieu of axillary or femoral sites
- Hand hygiene, preparation of skin for insertion, and exit site dressing recommendations as per central venous catheters
- Application of cap, mask, sterile gloves, and small sterile fenestrated drape during peripheral arterial line insertion
    - Addition of sterile gown and full-body sterile drape during insertion of an axillary or femoral arterial line
- Do not routinely replace arterial catheters to prevent infection
- Remove the arterial catheter as soon as it is no longer needed for patient care

coagulase-negative staphylococci, enterococci, or non-pseudomonas Gram-negative bacilli, treatment without catheter removal can be attempted. Systemic therapeutic antibiotics should be given for 10 to 14 days. Meanwhile, antibiotic lock solution, appropriate for the pathogen and for the catheter (ie, increased concentrations of some antibiotics are required when coadministered with heparin and lock solution volume varies by catheter type, length and lumen number) must be administered to every lumen, ideally daily with 24-hour dwell time. Dwell time can be extended to 48 hours or, in the case of tunneled hemodialysis catheters, to the intervals between maintenance dialysis sessions. Recommendations for antibiotic and anticoagulant concentrations are available and must be carefully adapted and administered to prevent under antimicrobial dosing and inadvertent systemic anticoagulation. If antibiotic lock solution cannot be administered, then the systemic antibiotic therapy must be administered through the infected catheter, rotating lumens of administration in the case of multilumen catheters. The catheter should be removed if there is evidence of clinical deterioration or ongoing bloodstream infection from catheter infection during antibiotic lock solution administration. Repeat blood cultures 1 week after completion of treatment is recommended for patients with long-term central venous hemodialysis catheters treated with antibiotic lock therapy for catheter salvage.[2]

Prevention

Evidence-based principle recommendations for preventing central venous arterial catheter related bloodstream infections are summarized in Tables 2 and 3. Additional recommendations for management of central venous, peripheral venous, and arterial lines to reduce risk of CRBSI are available.[8] Simultaneous application of multiple recommended practices at single centers has been associated with significant declines in the rates of these infections in quasi-experimental studies.[20–30] Bundling of recommended practices to ensure adherence to all of them during discrete episodes of care has further promoted prevention.[31,32] Optimization of multidisciplinary care to reduce risk of CRBSI

Table 4. The CLABSI by Unit Location Reported to NHSN in 2010.[38]

ICU Type (Number of Units)	Number of CLABSI/Number of Line Days	CLABSI Incident Density	
		Pooled Mean	Percentile 10, 25, 50 (Median), 75, 90
Medical, major teaching hospital (298)	660/372 229	1.8	0.0, 0.8, 1.4, 2.3, 3.5
Neurologic (24)	44/37952	1.2	0.0, 0.0, 0.6, 2.0, 3.2
Neurosurgical (95)	207/154 375	1.3	0.0, 0.0, 0.8, 1.6, 2.7
Surgical, major teaching hospital (127)	410/297 551	1.4	0.0, 0.4, 1.0, 1.9, 3.2

Abbreviations: CLABSI, central line-associated blood stream infection; NHSN, National Healthcare Safety Network; ICU, intensive care unit.

at the level of units within hospitals is being tested as another technique to reduce CRBSI incidence.[33] Finally, collaborations between facilities to enhance adoption of all processes of care intended to reduce risk of CRBSI[34,35] have been associated with significant declines in the frequency of these infections.

Surveillance and Reporting

Surveillance has been defined as a routine and orderly collection of data based on a standard definition of cases.[36] Hospital-based infection control teams begin surveillance for bloodstream infections by regularly reviewing results of blood cultures obtained at their facilities. The results of their surveillance have been used to detect outbreaks, to direct prevention activities, and more recently to measure quality of care.

As mentioned earlier, surveillance of CRBSI is complicated by differences in application of diagnostic strategies between providers, patients, units, and health care facilities that can lead to differences in frequency of CRBSI case finding. Surveillance for CLABSI in lieu of CRBSI addresses this problem, as cultures that indicate infection of a specific catheter are not required to meet the CLABSI case definition. Although surveillance for CLABSI is challenged by the potential for different application of its defining clinical criterion (ie, infection that cannot be attributed to infection at another body site) between infection control surveyors and facilities,[37] it has functioned with satisfactory stability of sensitivity and specificity of case detection between facilities to allow development of a database for benchmarking by the NHSN.[38]

Monthly at over 1000 hospitals across the country, infection control surveillance teams report the number of CLABSIs and the number of line days attributed to specific locations within their facilities to NHSN. As patient characteristics which are associated with risk of CRBSI and CLABSI cleave to hospital unit type (eg, neurologic ICU vs medical ICU vs surgical ICU, etc), reporting by unit location allows for risk stratification within the NHSN database. The incident density of CLABSI (number of CLABSI/number of 1000 central line days) at any unit of any hospital can be compared to comparable units of comparable hospitals within the NHSN database. The most recent report of pooled CLABSI surveillance data from neurologic ICUs, neurosurgical ICUs, and medical and surgical ICUs at major teaching hospitals are shown in Table 4.[38] Feedback of these risk-stratified, benchmarked CLABSI incident densities to hospitals by NHSN has been associated with declines in CLABSI incidence.[39]

A standardized infection ratio (SIR) is created by dividing the number of infections observed during a particular period of time by the number of infections that would have been expected by a benchmark. A SIR for CLABSI is created in NHSN for each ICU that reports CLABSI incidence data to NHSN.[40] Beginning January 2011, CMS has required acute care hospitals that wish to receive compensation under its conditions of participation program,[41] to report their ICU CLABSI incidence densities to NHSN, which are then displayed by SIRs on the CMS Hospital Compare Web site.[42]

Conclusion

Catheter-related bloodstream infections are costly complications of hospital care that have occurred with greater frequency in the ICU settings. Accurate diagnosis can be established by culture of appropriately collected specimens of blood and catheter tips. Evidence-based guidance is available to inform antibiotic treatment and catheter management when infection occurs. Risk of CRBSI can be reduced by optimizing catheter selection, insertion and maintenance, and by removing catheters when they are no longer needed.

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