Prevention of Central-Line Associated Bloodstream Infections: 2021 Update

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KEYWORDS
• Bloodstream infection • Intravascular catheter • Prevention • Bacteremia

KEY POINTS
• Central line-associated bloodstream infections and catheter-related bloodstream infections are responsible for substantial morbidity, mortality, and increased health care costs.
• Many of these infections are preventable using current knowledge and prevention techniques.
• Evidence-based strategies to prevent central line-associated bloodstream infections include decision-making about appropriate catheter choice and insertion bundles.
• Techniques to increase adherence to standard of care practices such as staff training, education, appropriate staffing levels, and leadership involvement are equally important in central line-associated bloodstream infections prevention.
• Health care–associated infections rates, including central line-associated bloodstream infections, have increased during the severe acute respiratory syndrome coronavirus 2 pandemic.

INTRODUCTION AND CLINICAL SIGNIFICANCE

Vascular catheter insertion is the most common procedure in hospitalized patients.¹ Intravascular catheters are used in a wide range of clinical settings for treatment including, but not limited to, delivering medications, obtaining blood samples, hemodynamic monitoring, and facilitating life-saving procedures such as extracorporeal membrane oxygenation and renal replacement therapy. All vascular catheters carry a risk of adverse events, with infectious complications ranging from local skin and soft tissue infection to more severe bloodstream infections (BSIs).² Catheter-related infections increase hospital costs, extend the length of stay, and increase the risk of death. An estimated 30,000 to 40,000 episodes of CLABSI occur yearly in the United States in acute care hospitals.³⁴ Preliminary data from the coronavirus disease 2019

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(COVID-19) pandemic demonstrate an increase in hospital-associated infections (HAIs), including vascular catheter-related infections.5

DEFINITIONS AND SURVEILLANCE

Defining infections owing to vascular catheters is complicated by the variety of catheter types and imprecise terminology used. For example, CLABSI is a term defined by the Centers for Disease Control and Prevention’s National Healthcare Safety Network.3 A CLABSI is defined as a BSI in a patient with a central venous catheter (CVC), without another attributable source of infection, that occurs when the CVC has been in place for more than 2 calendar days or removed the day before the BSI.3,6 CVCs can be inserted centrally, typically in the femoral, subclavian, or internal jugular veins, or peripherally in the cephalic or brachial veins (peripherally inserted central catheter [PICC]).3

CLABSI overestimates the rate of true infection and has inherent subjectivity by the requirement to assign the source of infection. Notably, midline catheters, arterial catheters, and peripheral intravascular catheters (PIVs) are excluded from the formal surveillance definition.3 Not only are the CLABSI definition and surveillance system used to establish benchmarks, they are used for interinstitutional comparison and to drive performance improvement and third-party hospital reimbursement.

The other commonly used term is catheter-related BSI (CRBSI). CRBSI is a clinical definition that uses microbiologic data such as catheter tip cultures, differential time to positivity, or quantitative blood cultures to diagnose, and causally attribute, a BSI to a specific vascular catheter.4 When evaluating the medical literature, it is important to not inadvertently interchange CLABSI and CRBSI.

Owing to the standardization of the CLABSI definition, it has become a common end point for both research and quality improvement studies and has been extrapolated and applied to non-CVC catheters. In the United States, efforts to decrease CLABSI rates have resulted in financial penalties for hospitals with rates of CLABSI that are higher than national targets. An increased interest in CLABSI prevention, at least partially driven by a desire to avoid financial penalties and preserve institutional reputation, has resulted in a robust literature on the topic. Unfortunately, fewer data exist regarding the prevention of BSI owing to non-CVC vascular devices.

PATHOGENESIS

Vascular catheters become inoculated through several mechanisms, and effective infection prevention techniques are needed to address each possible source. Contamination of the catheter can occur during insertion through inadequately disinfected skin of the patient, inadequate health care worker hand hygiene, or other deviations from standardized CVC insertion practices (ie, insertion bundle). Postinsertion lapses in dressing practices can result in dermal organisms gaining access to the catheter. While in place, the catheter hub and lumen may become contaminated, particularly if hub cleansing and hand hygiene are suboptimal, resulting in colonization and infection. Additionally, vascular catheters may become inoculated through hematologic spread from another site of infection, or rarely via contaminated infusates4 (Fig. 1).

Biofilms and Their Role in Infection

The recognition of the importance of biofilms, and their impact on infection, is continually increasing. Biofilms are a distinct community of microbes that produce an extracellular polymeric substance that facilitates irreversible adherence to surfaces, such
as the lumen of a vascular catheter. Biofilms provide opportunities for plasmid transfer between cells (bacterial conjugation) and cell-to-cell signaling (e.g., quorum sensing), which can increase the fitness of the micro-organisms and result in infections that are more difficult to eradicate. Bacterial colonization of vascular catheters, via mechanisms discussed elsewhere in this article, can occur in as little as 24 hours, with biofilms subsequently identified as quickly as 48 to 72 hours after catheter insertion. This finding is clinically significant because biofilms also decrease the effectiveness of the immune system’s phagocytes and complement system, and antibiotic susceptibility decreases around 1000-fold, causing further difficulty in eradication. The recognition of the importance of biofilms has led to technological innovations, such as the development of antimicrobial-coated CVCs designed to prevent, or limit, biofilm formation.

Once formed, infections with biofilms can be difficult to treat without removal of the infected catheter, so the prevention of biofilm formation is key to successful prevention of CRBSI. Historically, biofilms were associated with *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*, *Enterococcus* species, and coagulase-negative staphylococci. New pathogens are increasingly being recognized as biofilm formers, such as *Candida auris*, a known multidrug-resistant organism. Given the difficulty in treating biofilm infections, strategies other than conventional antibiotics are increasingly being explored, such as antibiofilm molecules that inhibit quorum sensing, dispersion of extracellular polysaccharide substance, and molecules that disrupt biofilm adhesion mechanisms, but are not yet all available commercially.

**PREVENTION OF INFECTIONS**

**Clinical Decision-Making Regarding Catheter Type and Necessity**

The first step in preventing vascular catheter infections is to optimize the choice of catheter based on the patient’s clinical need. Different types of catheters have variable risks of complications, including infections; thus, the type of catheter must be considered before insertion. Vascular access algorithms may aid teams in complex device selection decisions (Fig. 2). Patient comfort and ease of access should also be taken into account when deciding on the optimal vascular access device. Decreasing needle sticks, the possibility of complications, and the location of the vascular catheter...
are factors that should be discussed with the patient before placement, if feasible, in an opportunity for shared decision-making.\textsuperscript{11}

**Length of expected need**

Vascular catheters are viable for various lengths of time, from subcutaneously implanted ports that can be used for years, to PIVs that may only last a few days. CVCs can be tunneled if needed nonemergently or for more than 1 week, or nontunneled for emergent central access.\textsuperscript{11} PIVs are ideal if the anticipated patient need for vascular access is fewer than 6 days, and no other criteria for other central vascular access are met.\textsuperscript{11} Midline catheters (midlines) can stay in place for 2 to 4 weeks, and provide an option for de-escalation from a CVC when central access is no longer required. There is mixed evidence regarding whether midlines have rates of infection similar to PIV or PICC.\textsuperscript{12-15} Tunneled vascular catheters can remain in place for months.

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Selby et al
Implantable devices, such as ports, provide long-term vascular access and are often used for chemotherapy regimens requiring central access over months to years.

**Indications for therapeutic infusions**

Certain medications such as vasopressors and vesicant chemicals, such as some chemotherapeutic agents, are recommended to be administered via a CVC rather than through a PIV. Over time, the list of medications that can be safely given through PIVs has expanded. For example, as recently as 2011, vancomycin was included in the Infusion Nursing Standards of Practice as a medication to be given through a central catheter owing to its low pH.16 Multiple studies have now demonstrated that vancomycin can safely be given through a PIV or midline.11 This change illustrates the importance of regular review of hospital policy around infusate requirements, and clinician familiarity with those policies, when making decisions about vascular catheter placement.

**Patient monitoring**

Vascular catheters are also used to monitor hemodynamic parameters such as the central venous pressure and the pulmonary artery pressure. If hemodynamic monitoring is the primary reason for placement of a CVC, consider removal of the catheter, or de-escalation to a peripheral catheter, when monitoring of those hemodynamic parameters is no longer clinically necessary or when measuring through noninvasive methods is feasible.11

**Difficult vascular access**

Patients with difficult to obtain venous access may require CVC placement. In such cases, attempts to obtain noncentral access should be considered carefully before CVC placement. For instance, ultrasound guidance can be used to maximize successful cannulation of peripheral veins in patients with difficult or tenuous vascular access.17–19 Including the number of unsuccessful cannulation attempts before escalating to ultrasound guidance or recruitment of more experienced vascular access team personnel, and consideration for different types of vascular catheters in a hospital vascular access algorithm or policy is reasonable (see Fig. 2 for an example of a vascular access algorithm). When placing both centrally inserted central catheters and PICCs, guidelines recommend providers use real-time ultrasound guidance to increase the rate of successful placement and minimize complications.18

Additional factors to consider when deciding on what type of vascular access catheter is the best option for a particular patient includes chronic kidney disease status because PICCs can affect the long-term options for dialysis by contributing to central venous stenosis, which affects hemodialysis fistula placement.20 One study has suggested that patients with a prior history of PICC placements have an increased rate of PICC associated BSIs, so prior placement of PICCs could be considered as well.21 Finally, the number of lumens on a catheter should be minimized to what is needed for patient care, because more lumens increase the risk of infection and thrombosis.22

**CATHETER CHECKLIST AND BUNDLES**

Using a bundle, in which a variety of interventions are combined together for placement and after care of CVCs, has been documented in many studies and quality improvement projects to decrease rates of CLABSI and CRBSI.23–26 Bundles frequently consist of an insertion kit, hand hygiene, skin preparation, maximal barrier precautions, chlorohexidine-impregnated dressing, and checklist to ensure that all steps are performed.27 Maximal barrier precautions include using sterile gown and...
gloves, a surgical mask, head covering, and a sterile drape over the patient’s full body.27 Although the relative importance of each component of a bundle is not defined clearly, the bundled approach has proven successful in preventing CLABSIs.4 Based on this persuasive evidence, institutions should develop a bundle to decrease their rates of CLABSI and CRBSI. See Table 1 for bundle component considerations.

Types of Catheters and Techniques and Devices to Prevent Infection

Antimicrobial-coated catheters
CVCs have been coated or impregnated with a variety of antimicrobial agents and these have been shown to decrease CRBSI in adults and pediatric population.28,29 The most extensively studied CVC coatings are silver sulfadiazine/chlorhexidine and minocycline/rifampin.30 Some CVCs are coated on both the internal and external surfaces, whereas in others the material of the catheter itself is impregnated with the antimicrobial substance.29 The latter are typically metal-based antimicrobials such as a silver or platinum product.29 Nonantibiotic compounds are increasingly being investigated for the prevention of biofilm formation in medical devices, including vascular catheters.29

Using a coated CVC should be considered when the catheter is anticipated to be needed for more than 5 days. Guidelines also suggest that coated catheters can be used in hospital units when rates of CLABSI remain high despite other standard interventions or in patients who are considered high risk for CLABSI.29,30 Although concern for the development of antimicrobial resistance when using coated CVC catheters is understandable, there is no evidence to suggest that the use of these devices is associated with increased resistance rates.31 If an antimicrobial catheter is used, clinicians should be aware of the type of antimicrobial and what organisms are resistant to it, for example, minocycline/rifampin–coated catheters lack activity against *P. aeruginosa* and *Candida* spp.29

Hub cleaning, connectors, and accessing catheters
Scrubbing the catheter hub before accessing the catheter is crucial in decreasing risk for infection that is, “scrub the hub.”32 The minimal needed scrub time is not well-defined. However, 1 study demonstrated that a 15-second scrub with 70% isopropyl

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Evidenced-based practices for prevention of vascular access catheter infections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pericatheter Insertion</strong></td>
<td><strong>Devices and Technology</strong></td>
</tr>
<tr>
<td>Appropriate staffing</td>
<td>Antimicrobial catheter coatings</td>
</tr>
<tr>
<td>Education and training</td>
<td>Chlorhexidine impregnated dressings</td>
</tr>
<tr>
<td>Maximal sterile barriers</td>
<td>Passive port protectors</td>
</tr>
<tr>
<td>Insertion site selection</td>
<td>Silver-impregnated connectors</td>
</tr>
<tr>
<td>Cutaneous antisepsis</td>
<td>Sutureless catheter securement</td>
</tr>
<tr>
<td>Insertion checklist</td>
<td>Antimicrobial catheter locks</td>
</tr>
<tr>
<td>Bundle approach</td>
<td></td>
</tr>
<tr>
<td><strong>Postcatheter insertion</strong></td>
<td></td>
</tr>
<tr>
<td>Scrub the hub</td>
<td></td>
</tr>
<tr>
<td>Chlorhexidine patient bathing</td>
<td></td>
</tr>
<tr>
<td>De-escalation of unneeded catheters</td>
<td></td>
</tr>
<tr>
<td>Catheter dressing maintenance</td>
<td></td>
</tr>
<tr>
<td>Bundled approach</td>
<td></td>
</tr>
</tbody>
</table>
alcohol eliminated colonization of needleless connector surfaces with a high microorganism count and another showed no difference between 5-second and 15-second scrub times.\textsuperscript{33,34} Lever lock systems have been shown to have higher rates of bacterial colonization than luer lock catheter connectors.\textsuperscript{35} Some needleless connectors have been associated with an increased risk of infection, which may be related to their ease of disinfection.\textsuperscript{32} This issue is complex and most likely relates to a variety of needleless connector characteristics, such as fluid displacement, dead space, flow dynamics, material transparency, and perhaps most important, the design of the interface between the plastic components and the diaphragm contacting the catheter hub. Optimum design and function require an interface that can be readily disinfected in a short period of time.\textsuperscript{36}

Needless connectors impregnated with silver have also been associated with decreased rates of CLABSI.\textsuperscript{37,38} Standard precautions when accessing hubs and connectors, such as hand hygiene, should not be ignored; however, multiple studies have demonstrated, that despite education-driven initiatives, rates of nonadherence can still be high.\textsuperscript{22}

Alcohol-containing passive hub disinfection caps have been shown to decrease CLABSI in several studies and are being used increasingly as an additional CRBSI prevention strategy.\textsuperscript{22,35,39–41} Alcohol disinfection caps may also decrease blood culture contamination.\textsuperscript{37} Although now used widely, there are limited randomized controlled trials exploring the use of passive hub disinfection, with most trials being done in a quasiexperimental manner.\textsuperscript{22,39–41}

Closed intravenous infusions systems have been shown to have lower rates of CLABSI compared with open infusion systems. Open intravenous infusion systems use a glass bottle, burette, or semirigid plastic bottle and require external venting to allow fluid to exit the container and be infused to the patient.\textsuperscript{42} The infusate can become contaminated during the venting processes, and open systems have been tied to numerous outbreaks of gram-negative bacteremia.\textsuperscript{42} Closed systems include a fully collapsible bag that does not require venting, decreasing the risk of a contaminated infusate.\textsuperscript{42} Open systems are used more commonly in resource-limited settings, but if resources are available, a closed intravenous system decreased the risk of CLABSI and CRBSI.\textsuperscript{27,42}

**Dressing and dressing changes**

Several types of dressings for CVCs are available. Sterile gauze dressings should be changed every 48 hours, and transparent semipermeable dressings weekly.\textsuperscript{34,43,44} Soiled, loose, or damp dressings should be changed promptly, to prevent an increased risk of CLABSI.\textsuperscript{34,44} Chlorhexidine-impregnated dressings can decrease micro-organisms at the insertion site of a CVC and have well-documented usefulness in the prevention of CRBSI for adults with short-term, nontunneled CVCs.\textsuperscript{45,46} In general, administration sets should be changed no more than every 96 hours. Exceptions to the 96-hour administration set change recommendation include the following: parenteral nutrition administration sets should be changed every 24 hours, and those used to administer blood every 4 hours or at the completion of a unit.\textsuperscript{34}

**Antimicrobial locks**

Antimicrobial lock is a process in which the lumen of a catheter is filled with an antimicrobial solution for a set duration. Antimicrobial lock solutions may contain antibiotics, antiseptics, or compounds directed toward preventing bacterial adherence or biofilm formation. Primarily studied in patients requiring longer term vascular catheters or patients with prior episodes of CRBSI, and sometimes as part of an attempt to
salvage an already infected catheter, there is growing evidence that lock therapy is effective in CRBSI prevention. The ideal dwell time, best choice of antimicrobial solution, and potential complications remain in question. The risk of antimicrobial resistance and lumen integrity when lock therapy is used prophylactically are areas that especially need additional exploration. A study published in 2019 demonstrated that antimicrobial lock therapy to prevent CLABSI resulted in an overall cost savings when used in hemodialysis settings, oncology treatment, or home parenteral nutrition. Antimicrobial lock therapy for CLABSI prevention should be considered on a case-by-case basis, and more strongly considered in long-term vascular catheter use or in patients with prior CRBSI, including pediatric patients.

Chlorhexidine gluconate baths
Multiple studies have shown that chlorhexidine gluconate baths decrease the rate of CLABSI. The majority of studies have been performed in critical care settings; however, there is reasonable evidence to suggest that daily chlorhexidine gluconate baths in patients with CVCs outside of the intensive care unit also have lower rates of CLABSI and CRBSI, and therefore should be considered in noncritical care patients. The widespread use of chlorhexidine for bathing and methicillin-resistant S aureus decolonization has led to concern that resistance to chlorhexidine may be developed. Low-level resistance of S aureus to chlorhexidine, called tolerance, occurs by efflux pumps mediated by the qacA and qacB genes. The clinical significance of tolerance remains unclear, although some evidence suggests that S aureus strains with these genes are associated with health care exposure. No clinically significant resistance to chlorhexidine has been attributed to chlorhexidine gluconate bathing, but this area continues to be investigated.

Implementing Standard of Care Practices to Prevent Infection
As vascular catheter infection prevention practices have become more standardized, there has been a growing body of implementation and dissemination research exploring the barriers to implementing evidence-based practices and increasing adherence to safe practices in all aspects of vascular catheter care.

Staffing
Several studies have demonstrated that the understaffing of hospital units has contributed to higher rates of CLABSI. All levels of health care professionals play a role in vascular catheter infection prevention, and when staffing is inadequate, it can lead to increased rates of infection. Because all hospital units have unique staffing needs, from an infection prevention perspective, it is impossible to recommend exact staff to patient ratios, other than that staffing should be adequate to follow all recommended practices. High rates of health care worker burnout have also been associated with increased risk of HAIs; thus, resiliency and wellness should be considered in the strategic planning of preventative initiatives. Robust vascular access teams have also been associated with lower CLABSI rates, presumably through greater adherence to recommended practices from a dedicated team.

Training and education
Adequate training and continuing education in the insertion and care of vascular catheters has been shown to decrease the rates of catheter infection. One study showed that, after the implementation of a CLABSI prevention bundle, the rate of infection did not decrease until adherence of individual bundle elements was more than 95%, highlighting the importance of training and education in catheter-related infection prevention. Quality improvement initiatives focusing on hand hygiene and catheter
hub cleaning have been associated with decreased rates of CLABSI, demonstrating that effective CLABSI prevention may not require substantial upgrades to medical technology.64 Interventions targeted directly to units with high CLABSI rates can show substantial decreases in infection rates and improvement in staff knowledge and protocol adherence when providing care.65 Various methods of continuing education have found success at decreasing catheter infection rates, including classroom-based interventions, simulations, yearly skills checks, and the use of bedside observers and educators.66 A robust multidisciplinary education program to optimize adherence to bundle guidelines and hospital vascular catheter policy should be a part of every hospital system infection prevention program.

Role of leadership involvement in catheter infection prevention
For successful prevention of vascular catheter infections, engagement of senior administrative leadership is necessary. A study conducted at 18 hospitals across the United States found that executive leadership engagement and manager coaching promoted prevention of HAI including CLABSI.67 Although perhaps not feasible for all hospital systems, the involvement of executive leadership in hospital units reporting a CLABSI to provide feedback and goal setting can assist with prevention.68

Practices to de-escalate vascular catheters
De-escalation when a certain type of catheter is no longer indicated clinically is an important infection mitigation strategy. A multimodal strategy is needed to assist with clinically indicated de-escalation. Because vascular catheters are often hidden under clothing or blankets, clinicians can be unaware of the presence of a vascular catheter, which can be a barrier to removal.59 Tools in electronic health records can be used to alert clinical staff to the length of time a catheter has been in place, but often need to be optimized to give accurate and easy to find information about catheters.59

In a critically ill patient with complex medical problems, vascular catheter de-escalation can be inadvertently deprioritized by medical providers. However, a discussion about the continued need for a CVC should occur daily among the medical team.10,71 Checklists for use during rounds by the medical team in intensive care units are now common and should include vascular catheter considerations. It should be noted that the addition of a checklist alone has not been shown to decrease the rates of CLABSI, and checklists are but a single valuable tool in multimodal CLABSI prevention programs.72

For patients outside of the acute hospital setting who require vascular access for monitoring or medication administration, vascular catheters should also be removed when no longer needed. Limited data are available about rates of failure to remove ports or other long term type devices, but clinicians should monitor for continued need at regularly scheduled intervals.

EFFECTS OF THE SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 PANDEMIC ON VASCULAR CATHETER INFECTIONS
Since the start of the severe acute respiratory syndrome coronavirus 2 pandemic, several studies have reported increased rates of CLABSI and BSI in both COVID-positive and non–COVID-infected individuals in intensive care units.73–75 Prolonged intensive care unit admissions for patients with COVID-19, with more catheter days per patient does increase each patient’s individual CLABSI risk. However, the CLABSI rate, which is expressed per 1000 CVC days, should not increase based solely on catheter dwell time. There is evidence to suggest that staffing shortages may be a
strong factor, because lower nurse to patient ratios allows less time to maintain standard of care maintenance of catheters.\textsuperscript{74,76} Health care worker burnout, which has been associated with increased risk of HAI and has been shown to have increased with the pandemic, could also be contributing.\textsuperscript{59,77} Additionally, changes in behaviors such as moving intravenous pumps outside of rooms to minimize health care staff from entering patient rooms resulted in long tubing extensions, more tubing connectors, and an increased number of possible contamination sites.\textsuperscript{73} The increase in prone position ventilation (patient lying face down for up to 16 hours per day, as opposed to traditional supine positioning) may make it more difficult to access vascular catheters or assess dressing integrity could also be contributing to increasing rates. Some data suggest\textsuperscript{73} that more CVCs were placed emergently in patients with COVID-19, and higher rates of femoral catheters were used during the COVID-19 pandemic, both of which have been associated with higher rates of infection.\textsuperscript{43,74}

Finally, the COVID-19 pandemic has resulted in a reallocation of infection prevention and antibiotic stewardship resources toward COVID-19–related issues, resulting in a neglect of other infection control efforts, which may have further exacerbated the increase in vascular catheter infections.\textsuperscript{78}

\textit{Special Subgroups of Patients to Consider}

\textbf{Vascular access at home}

Vascular catheter access can be required for multiple purposes outside of the acute care hospital, including home parental nutrition, outpatient antibiotic therapy, and access for administration of fluids or chemotherapy regimens.\textsuperscript{79} The majority of research done about the prevention of CLABSI and CRBSI have been done in the acute care and critical care setting. There is a small but growing body of literature about surveillance and prevention in the home therapy setting.\textsuperscript{80} Using data collected through home health care agencies that provide in-home care for patients with CVCs has been used to track rates of CLABSI in small studies, but there can be variability in definitions used to define CLABSI in home infusion therapy.\textsuperscript{81} When surveyed about how CLABSI is defined, many home infusion nurses used provider documentation or a positive CVC tip culture as the sole means of defining CLABSI, although neither of these is consistent with the CLABSI definition used in the acute care setting.\textsuperscript{81} Adherence to CLABSI/CRBSI infection prevention practices has not been well-studied in the home care setting.\textsuperscript{82}

\textbf{Patients with hematologic malignancies}

Patient receiving cytotoxic chemotherapy that results in myelosuppression are at high risk of HAIs, including CLABSI.\textsuperscript{52} Although the majority of infection prevention strategies for patients with hematologic malignancies are similar to other patients, multiple studies have examined additional prevention techniques to reduce infection in this high-risk group.\textsuperscript{30} Chlorhexidine gluconate baths in patients outside of the intensive care unit have been shown to decrease health care–associated BSI owing to gram-positive bacteria in hematologic malignancy patients, in contrast with studies for all patients outside of the critical care setting, which has demonstrated mixed results.\textsuperscript{52}

\textbf{Arterial catheters}

Arterial catheters are often placed under less stringently aseptic conditions than CVCs, and are often not tracked in CLABSI or CRBSI reporting systems.\textsuperscript{85} However, studies have shown that arterial catheters have similar infection rates to CVCs.\textsuperscript{84} Based on this finding, it would be reasonable to track and report BSI associated with arterial catheters and consider interventions to decrease rates.\textsuperscript{4}
SUMMARY

Vascular catheters remain a significant source of infection despite robust research in the field of prevention. Surveillance should include all nosocomial BSIs, including PIVs, midlines, and arterial catheters, with CLABSI as a subset within the surveillance plan. Efforts to decrease BSIs from all vascular catheters portends improved outcome and costs for patients and health care organizations. Recently, the increase in CLABSIs during the COVID-19 pandemic demonstrates the continued need for research to prevent future morbidity, mortality, and cost associated with these infections, as well as research to increase adherence to proven strategies.

CLINICS CARE POINTS

- Optimal vascular access decision-making is critical and must include consideration for type of catheter needed, duration of need, and clinical indications for use.
- De-escalation of catheters is another key aspect in catheter-related risk reduction, including transitioning to a peripheral intravenous or midline as soon as central access is no longer required.
- Process improvements, including workflow, education, and the use of bundled approaches, may improve adherence to evidence-based practices across all spectrums of catheter care.
- If higher CLABSI rates persist, assess adherence to standard practices and consider implementation of coated catheters and universal chlorhexidine gluconate baths.

DISCLOSURE

The authors report no conflicts of interest related to this article. Dr M.E. Rupp reports having served as a consultant for 3M, Becton-Dickinson, Teleflex, and Citius Pharmaceuticals.

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