Prevention of Catheter Related Bloodstream Infection

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INTRODUCTION

Intravascular catheters play a role in the daily management of almost all our patients. These devices allow us to administer intravenous fluids, medication and parenteral nutrition, and provide access for haemodialysis and haemodynamic monitoring. Although one of the most important innovations in modern medicine, these devices are not without complications, one of the most serious being infection.

Between 2006 and 2007, the National Health and Safety Network in the United States determined that the mean rate of central line associated blood stream infection was 1.3 to 5.6/1000 catheter days.\(^1\)

The Centers for Disease Control and Prevention have found that catheter related blood stream infection (CRBSI) is one of commonest sites of nosocomial infection in the United States. They found that 80,000 CRBSI occur in Intensive Care Units annually, with a total number of 250,000 if the entire hospital population is assessed.

CRBSI increase hospital costs by almost $3 billion annually. There is considerable morbidity and mortality. The estimated number of deaths is 14,000 per year. The length of hospital stay in the survivors is prolonged by 1 week.\(^2\)

Many health care insurance programs in the United States no longer reimburse health care institutions for the cost of CRBSI, as it is a potentially avoidable or ‘never’ complication of intravascular catheters.

Based on the enormous medical and financial impact, an aggressive multidisciplinary approach is urgently needed to prevent CRBSI.
**DEFINITIONS**

**Intravascular Catheter**
It is a device that is introduced into and resides in a blood vessel. There are many different ways of describing intravascular devices, for example, according to the type of vessel it occupies, its site of insertion, its physical length, its pathway from the skin to the vessel, its intended duration of use or some unique characteristic of the catheter.

**Catheters used for venous and arterial access.** [3]

<table>
<thead>
<tr>
<th>Catheter type</th>
<th>Entry Site</th>
<th>Length</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral venous catheters</td>
<td>Usually inserted in veins of forearm or hand</td>
<td>&lt;3 inches</td>
<td>Phlebitis with prolonged use; rarely associated with bloodstream infection</td>
</tr>
<tr>
<td>Peripheral arterial catheters</td>
<td>Usually inserted in radial artery; can be placed in femoral, axillary,</td>
<td>&lt;3 inches</td>
<td>Low infection risk; rarely associated with bloodstream infection</td>
</tr>
<tr>
<td></td>
<td>brachial, posterior tibial arteries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midline catheters</td>
<td>Inserted via the antecubital fossa into the proximal basilic or cephalic</td>
<td>3 to 8 inches</td>
<td>Anaphylactoid reactions have been reported with catheters made of elastomer hydrogel; lower rates of phlebitis than short peripheral catheters</td>
</tr>
<tr>
<td></td>
<td>veins; does not enter central veins, peripheral catheters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nontunneled central venous catheters</td>
<td>Percutaneously inserted into central veins (subclavian, internal jugular, or femoral)</td>
<td>≥8 cm depending on patient size</td>
<td>Account for majority of CRBSI</td>
</tr>
<tr>
<td>Pulmonary artery catheters</td>
<td>Inserted through a Teflon(^*) introducer in a central vein (subclavian, internal jugular, or femoral)</td>
<td>≥30 cm depending on patient size</td>
<td>Usually heparin bonded; similar rates of bloodstream infection as CVCs; subclavian site preferred to reduce infection risk</td>
</tr>
<tr>
<td>Peripherally inserted central venous catheters (PICC)</td>
<td>Inserted into basilic, cephalic, or brachial veins and enter the superior vena cava</td>
<td>≥20 cm depending on patient size</td>
<td>Lower rate of infection than nontunneled CVCs</td>
</tr>
<tr>
<td>Tunneled central venous catheters</td>
<td>Implanted into subclavian, internal jugular, or femoral veins</td>
<td>≥8 cm depending on patient size</td>
<td>Cuff inhibits migration of organisms into catheter tract; lower rate of infection than nontunneled CVC</td>
</tr>
<tr>
<td>Totally implantable</td>
<td>Tunneled beneath skin and have subcutaneous port accessed with a needle; implanted in subclavian or internal jugular vein</td>
<td>≥8 cm depending on patient size</td>
<td>Lowest risk for CRBSI; improved patient self-image; no need for local catheter-site care; surgery required for catheter removal</td>
</tr>
<tr>
<td>Umbilical catheters</td>
<td>Inserted into either umbilical vein or umbilical artery</td>
<td>≤6 cm depending on patient size</td>
<td>Risk for CRBSI similar with catheters placed in umbilical vein versus artery</td>
</tr>
</tbody>
</table>
Catheter Colonisation

Catheter colonization is defined as a quantitative catheter tip culture yielding at least $10^3$ colony-forming units/mL. [4]

Catheter Related Blood Stream Infection

Two definitions:
Derived from clinical studies:

The same organism (determined by antibiogram or DNA typing) is retrieved from blood and the catheter tip, without evidence of infection with the identical organism at a different site. [1]

In the clinical setting:
The same organism is cultured from blood and the catheter tip and there is no evidence of infection with the same organism at any other site in the body. [3]

The problem with these definitions is that it is often difficult to determine if the blood stream infection is due to the catheter for multiple reasons:

- Catheters are not always removed to allow for microbiological testing
- Poor procedural compliance by staff e.g. incorrect labelling of specimens, lost specimens
- Limited availability of microbiological testing methods
- Overestimation of the true incidence of CRBSI as blood stream infection can occur from other undocumented sources

Central line associated bloodstream infection

It is a primary blood stream infection in a patient that has a central line within 48 hours before the development of the blood stream infection and is not related to an infection at another site. [3]
CRBSI occurs when the catheter becomes colonised by contaminating organisms. This occurs on the external surface (early colonisation) and internal luminal surface (late colonisation).

There are four possible routes for contamination of catheters in order of frequency:
1. Migration of organisms from the insertion site into the cutaneous catheter tract and along the outer surface of the catheter with colonisation of the catheter tract
2. Direct contamination of the catheter or catheter hub by contaminated hands, fluids or devices
3. Haematogenous seeding from another focus of infection
4. Infusion of contaminated infusate

Organisms colonise the surfaces of the catheter by forming a biofilm. The formation of biofilm is influenced by different factors:

- Material from which the catheter is made
  Catheters made from material with uneven surfaces result in enhanced adherence of organisms to the surface, making them more vulnerable to colonisation. Silastic catheters are more likely to be covered by a fibrin sheath that polyurethane catheters, again enhancing organism adherence. Some catheters are more thrombogenic than others and the formation of clot facilitates organism adherence to the catheter surface.

- Protein adhesions formed on the catheter by the host
  Fibrin and fibronectin form a sheath around the catheter, creating an environment for organism binding and adherence.

- Intrinsic virulence factors of the infecting organism
  Some organisms, like S. Aureus, express clumping factors that bind to host proteins on the catheter surface. Many organisms form a biofilm matrix or slime, in which they can embed themselves, thus making them less vulnerable to host defence mechanisms and antimicrobials.
CAUSATIVE ORGANISMS

Incidence rates, distribution of pathogens and crude mortality rates for patients in ICU.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>BSIs per 10,000 admissions</th>
<th>Percentage of BSIs (rank)</th>
<th>Crude mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n = 20,978) ICU (n = 10,515) Non-ICU ward (n = 10,442)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoNS</td>
<td>15.8</td>
<td>31.3 (1) 35.9 (1) 26.6 (1)</td>
<td>20.7 25.7 13.8</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10.3</td>
<td>20.2 (2) 16.8 (2) 23.7 (2)</td>
<td>26.4 34.4 18.9</td>
</tr>
<tr>
<td>Enterococcus species</td>
<td>4.6</td>
<td>9.4 (3) 9.8 (4) 9.0 (3)</td>
<td>33.9 43.0 24.0</td>
</tr>
<tr>
<td>Candida species</td>
<td>4.6</td>
<td>9.0 (4) 10.1 (3) 7.9 (4)</td>
<td>39.2 47.1 29.0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>2.8</td>
<td>5.6 (5) 3.7 (9) 7.6 (5)</td>
<td>22.4 33.9 16.9</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>2.4</td>
<td>4.8 (6) 4.0 (7) 5.5 (6)</td>
<td>27.8 37.4 20.3</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2.1</td>
<td>4.3 (7) 4.7 (5) 3.8 (7)</td>
<td>38.7 47.9 27.6</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>1.9</td>
<td>3.9 (8) 4.7 (6) 3.1 (8)</td>
<td>26.7 32.5 18.0</td>
</tr>
<tr>
<td>Serratia species</td>
<td>0.9</td>
<td>1.7 (9) 2.1 (9) 1.3 (10)</td>
<td>27.4 33.9 17.1</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>0.6</td>
<td>1.3 (10) 1.6 (10) 0.9 (11)</td>
<td>34.0 43.4 16.3</td>
</tr>
</tbody>
</table>

NOTE. Bacteroides species (n = 150; 1.4% of isolates) ranked ninth in non-ICU wards, CoNS, coagulase-negative staphylococci.

a  P < .05 for patients in ICUs vs. patients in non-ICU wards.

b  Significantly more frequent in patients without neutropenia.

c  Significantly more frequent in patients with neutropenia.

Thirteen percent of all episodes of blood stream infections are polymicrobial. The most frequent causative organisms are coagulase-negative Staphylococci (31%), Staphylococcus Aureus (20%), Enterococcus species (9%), and Candida species (9%). Infection with non-albicans species of Candida that are less responsive to azoles and Candida Albicans resistant to azoles are becoming more frequent. [1]
There is an increasing trend of infection with multidrug resistant organisms.

Rates of antimicrobial resistance rates over time among gram-positive isolates (methicillin-resistant *Staphylococcus aureus* [MRSA], methicillin-resistant coagulase-negative staphylococci MRCoNS), vancomycin-resistant *Enterococcus faecium* [VRE], ampicillin-resistant *Escherichia coli* [E. coli], and ceftazidime-resistant *Pseudomonas aeruginosa* [PSAE]) recovered in a series of 24,179 cases of nosocomial bloodstream infection

On-going surveillance is essential to determine the species distribution and antimicrobial susceptibility of organisms in respective units. This allows us to appropriately institute empirical therapy if a CRBSI is suspected. There is evidence to show that inappropriate empirical antibiotic therapy increases mortality rates from 30% to 60% in ICU patients. [6]

**DIAGNOSIS**

Diagnosis of CRBSI is a clinical dilemma. Unfortunately, it is rare for CRBSI to be associated with inflammatory signs at the insertion site, although when present it is a fairly reliable predictor of line sepsis. Clinicians should consider the diagnosis in patients with fever, hypotension, leukocytosis, or other signs and symptoms of sepsis. There is some suggestion that the resolution of signs of infection within 24 hours of catheter removal also correlates with CRBSI diagnosis.

CRBSI is suspected if there are symptoms and signs of infection 48 hours post insertion of an intravascular catheter.
There are two approaches to the diagnosis of CRBSI: the classical method, where the catheter is removed and tested, or a more conservative technique, where the suspected catheter is left in situ, and samples are taken from and around it.

The classical method is the quantitative culture of the catheter tip using the roll tip method. The catheter is removed after the skin surrounding the catheter insertion site is scrubbed with 2% chlorhexidine, and the distal 5cm is cut off with a pair of sterile scissors. The test is positive if >15 colony forming units (CFU)/plate, of the same organism cultured from the tip, is concomitantly isolated in a peripheral blood sample.

Between 23-37% of catheter tips cultured are sterile, with some studies finding that more than 50% of catheters withdrawn are culture negative. [4, 7, 8] Although there is a relationship between catheter colonisation and subsequent CRBSI, catheter colonisation does not always lead to CRBSI. Therefore, removal of the catheter without sufficient proof of CRBSI can result in unnecessary catheter removal and potentially increased risk of complications with insertion of a new catheter. Furthermore, some CRBSI in haemodynamically stable patients can be handled with the catheter in situ, using antibiotic or antiseptic lock therapy. Frequently, bacteraemia is cleared and the catheter is sterilized, following antimicrobial therapy.

The conservative techniques allow the suspected catheter to be investigated with the catheter in situ. There are three methods commonly used. [4]

- **Semi-quantitative superficial cultures.**

  In this method, a 3cm area of the skin around the catheter insertion site is swabbed and an alginate swab is taken from the inner surface of the catheter hub of all the lumens. Significant colonisation is when more than 15 CFU are cultured. A negative skin and hub culture almost completely excludes the catheter as the source of the bloodstream infection with a negative predictive value of 96.4%. It is easy to perform, cheap and widely available, making it a good screening tool. A positive result doesn’t imply that the catheter is the source of the infection, and this method has a low positive predictive value of 61%.

- **Differential quantitative blood cultures.**

  Ten millilitres of blood are taken from each catheter lumen and a peripheral venous site in a sterile fashion. A positive result is when the number of CFU/ml of blood from the catheter is 5X greater than the peripheral blood sample. This test has a high specificity (97.7%) and positive predictive value (83.3%). The drawbacks of this method are: it may only test the intraluminal surface of the catheter, potential catheter contamination, it is tedious to perform, laboratory personnel are exposed to blood, there is frequent contamination of the sample and it is expensive.
• Differential time to positivity.

Differential time to positivity is the difference in time needed for blood samples drawn simultaneously through the catheter hub and from a peripheral vein to yield positive culture results. Ten millilitres of blood is drawn simultaneously from the hub of each catheter lumen and a peripheral vein in an aseptic fashion. The culture bottles are appropriately labelled and taken immediately to the laboratory. It is then placed in an automatic culture detector which records culture positivity every fifteen minutes according to changes in florescence related to microbial growth.

A positive result is when the blood drawn from the catheter yields growth at least 120 minutes earlier than the peripheral blood sample. This technique has a high sensitivity (96.4%) and negative predictive value (99.4%). The drawbacks are: potential catheter contamination, the microbiology lab must be alerted beforehand and the specimens must be incubated immediately.

Comparison of the validity values (95% CI) of 3 techniques for the detection of catheter-related bloodstream infection. [4]

<table>
<thead>
<tr>
<th>Measure</th>
<th>Semiquantitative superficial cultures(^{a,b})</th>
<th>Differential quantitative blood cultures(^{a,c})</th>
<th>Differential time to positivity(^{a,c})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>78.6 (59.0–91.7)</td>
<td>71.4 (51.3–86.8)</td>
<td>96.4 (81.7–99.9)</td>
</tr>
<tr>
<td>Specificity</td>
<td>92.0 (87.0–95.6)</td>
<td>97.7 (94.3–99.4)</td>
<td>90.3 (85.0–94.3)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>61.1 (43.5–76.9)</td>
<td>83.3 (62.6–95.3)</td>
<td>61.4 (45.5–75.6)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>96.4 (92.4–98.7)</td>
<td>95.6 (91.4–98.1)</td>
<td>99.4 (96.6–99.9)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>90.2 (85.3–93.9)</td>
<td>94.1 (90.0–96.9)</td>
<td>91.2 (66.4–94.7)</td>
</tr>
</tbody>
</table>

**NOTE.** P<.05 was considered to be statistically significant.

\(^{a}\) P values for the comparison of validity values between semiquantitative superficial cultures and differential quantitative blood cultures were: sensitivity, .75; specificity, .01; positive predictive value, .09; negative predictive value, .79; and accuracy, .15.

\(^{b}\) P values for the comparison of validity values between semiquantitative superficial cultures and differential time to positivity were: sensitivity, .13; specificity, .81; positive predictive value, .99; negative predictive value, .12; and accuracy, .83.

\(^{c}\) P values for the comparison of validity values between differential quantitative blood cultures and differential time to positivity were: sensitivity, .04; specificity, <.001; positive predictive value, .10; negative predictive value, .04; and accuracy, .29.

Overall, the most accurate test is differential quantitative blood cultures, followed by differential time to positivity and then semi-quantitative superficial cultures. However, there is no statistical difference between the different test results. Therefore, convenience, availability of resources and local expertise should determine the technique chosen.
Identification of risk factors is essential as it allows us to implement preventative strategies to reduce the risk of CRBSI. There are a multitude of risk factors that may predispose a patient to developing CRBSI.

Factors related to patient characteristics.

Patients at extremes of age are more likely to develop CRBSI. However, paediatric patients exhibit a lower rate of infection with increased duration of catheterisation, probably as a result of decreased incidence of phlebitis. [2] The type of patient also influences the risk of CRBSI with the risk being highest in burns, trauma, paediatric and surgical patients.

Underlying diseases such as malignancy, immunodeficiency, cardiac failure, renal failure, COPD and liver disease may also predispose a patient to CRBSI, although studies investigating these factors have not shown them to be statistically significant. [9]

The severity of illness is also associated with CRBSI, with CRBSI occurring more frequently in patients with higher APACHE scores.

Patients with a tracheostomy are at a higher risk of developing CLABSI. It is hypothesised that this may be due to proximity of the line to the tracheostomy site with contamination. It could also be because of increased length of hospital stay with increased skin flora. Patients requiring ventilatory support are also more likely to develop CRBSI. [9]
Factors related to catheter insertion.

The rate of infection occurs, in decreasing order of frequency, in the femoral area, internal jugular vein, subclavian vein and peripheral sites respectively. The reason for increased incidence of CRBSI in the femoral region is thought to be due to increased skin flora in that region and the body habitus of the patient, with skin creases and an abdominal apron making hygiene difficult, especially in obese patients.

There is also a higher rate of catheter related venous thrombosis that may create an environment that facilitates organism adhesion to the catheter surface. In the paediatric population, there is a lower rate of mechanical and infectious complications associated with femoral catheters as compared to adults.

The subclavian vein appears to be the preferable site to avoid CRBSI; however, it is not without problems. There is a greater chance of mechanical complications, like pneumothorax, and it may lead to subclavian vein thrombosis and stenosis that makes vascular access in patients requiring haemodialysis difficult.

Some studies have shown no difference in the risk of infection between the three common sites, and suggested that catheter maintenance and early removal of catheters are possible reasons for this. [3, 9]

Catheters should be inserted as far away from wound sites as possible to minimize the risk of infection. Studies done in burn patients comparing catheter insertion site within 25cm² of burn wounds( near open wound) and more than 25cm² of burn wound(far from open wound) revealed that there was a greater incidence of catheter colonisation and a heavier organism load in catheters inserted near open wounds due to increased skin flora concentration in this area. [10]

Ultimately, the site of catheter insertion is determined by patient comfort, ease of maintenance of the catheter, relative risk of mechanical complications (pneumothorax and bleeding), patient specific factors (pre-existing catheters, bleeding diathesis, anatomic abnormalities), risk of infection and operator experience.

The vessel that the catheter occupies also contributes to the risk of infection, with the lowest risk being in peripheral venous catheters and peripherally inserted central venous catheters. It was also believed that arterial catheters have a lower risk of infection compared to central venous catheters. Lucet et al [11] have found this to be incorrect. In this study, the rate of catheter colonisation and CRBSI did not differ between arterial and central venous catheters. Additionally, the daily risk for infection of central venous catheters was constant over time after the fifth catheter day, but increased significantly over time after the seventh day for arterial catheters.
The spectrum of causative organisms was the same in each group. In this study, both catheters were inserted under the same aseptic fashion, thus excluding break in aseptic technique as a possible reason for the higher infection rate. It may be because of increased manipulation and repeated aspiration of blood with arterial catheters, and laxer maintenance with regard to skin care and dressing of the arterial catheter. Does this mean that we should be changing arterial catheters more routinely? Is the risk associated with infection higher than the risk of mechanical complications? More studies are needed to determine if routine arterial catheter changes decrease the rate of CRBSI with arterial catheters.

Daily hazard rate for catheter colonisation. [11]

Catheter exchange over a guide wire is an independent predictor of CRBSI. Possible reasons may be due to contamination of the guide wire by the colonised intraluminal surface of the catheter or from skin flora contaminating the cutaneous tract. Guide wire exchanges should be limited to patients where the risk of mechanical complications is high, or where there is limited venous access. [9]

The method and difficulty of insertion affects the rate of CRBSI, with risk of infection being proportional to the number of attempts at cannulation of the vessel, reflecting the difficulty of the procedure.

This may be due to multiple insertions of the needle breaching the skin, or due to contamination of the procedure field, equipment or operator. A meta-analysis by Hind et al [12] showed that the number of attempts at cannulation and complications were decreased with use of ultrasound to identify the internal jugular vein.
Two dimensional ultrasound was found to be superior to Doppler ultrasound. Use of ultrasound to locate the subclavian vein was associated with more attempts at cannulation and complications. Operator experience also determines the number of attempts at cannulation, mechanical complications and infection rates. Less experience operators are also less likely to adhere to an aseptic technique.

Catheters inserted in an emergency setting, as defined as insertion outside of ICU and during the night, have a higher incidence of CRBSI. This is most likely due to poor aseptic technique. It is recommended that lines inserted in an emergency setting be changed as soon as the patient is stable or within 48 hours of insertion. Hand washing, barrier precautions and skin preparation with antiseptics prior to catheter insertion are the most effective ways of preventing CRBSI. Cherry-Bukoweic et al [13] showed that best practice implementation with regard to aseptic technique was sufficient to keep infection rates at a minimum, without the need for other interventions.

Factors related to catheter characteristics.

Catheter material is an important determinant in the prevention of CRBSI. The material should be biocompatible, haemocompatible, biostable, chemically neutral and not altered by administered drugs. Furthermore, the catheter must be flexible, resistant, as radio-opaque as possible, thin walled with a high internal to external diameter ratio, resistant to sterilization, and with locked connections.

Polyurethane or Teflon® catheters have a lower risk of infectious complications compared to catheters made of polyvinylchloride (PVC) or polyethylene. Colonisation is higher in PVC catheters with a higher percentage of coagulate negative staphylococci, compared to Teflon® [14].

Studies comparing catheters with multiple lumens to ones with a single lumen show that catheters with multiple lumens have a higher incidence of infection. [15]

However, a recent meta-analysis by Dezfulian et al [16] shows that it may not necessarily be the actual number of lumens a catheter has that increases the risk of infection, but the variables associated with the choice of a multi lumen catheter, like severity of illness and the number of manipulations of the catheter for infusate administration and blood sampling.

Catheters coated with antimicrobial or antiseptic agents decrease microorganism adhesion and biofilm production, and hence, the risk of CRBSI. The use of such catheters may potentially decrease hospital costs, despite the additional acquisition cost of the coated catheter. There are two generations of these catheters. The first generation catheters are coated on the outer surface and the second generation catheters are coated on the outer and inner surface. There are three types of coatings currently available: chlorhexidine/silver sulfadiazine (CSS) coated, minocycline/rifampin (MR) coated and platinum/silver (PS) coated.
CSS and MR coated catheters show a lower rate of colonisation and infection compared to uncoated catheters. When compared with each other, the second generation MR catheters proved superior to the first generation CSS catheters, however they have not been compared to the second generation CSS catheters. Studies investigating PS coated catheters are conflicting, with some showing a decrease in infectious complications and others showing no difference to uncoated catheters. Potential adverse effects of coated catheters are anaphylactic reactions, which have been described with CSS catheters, and the risk of resistance to antimicrobials with MR catheters.

The antimicrobial or antiseptic coating may also interfere with diagnostic microbiological tests, giving false negative results.\(^\text{[17]}\)

**Factors related to catheter duration.**

The risk of infection increases steadily in relation to the number of days that the catheter is in situ. Early removal of catheters that are no longer necessary prevent CRBSI and decrease the morbidity and mortality from proven CRBSI. Garnacho-Montero et al \(^\text{[9]}\) found that the median time from insertion of the catheter to the development of bacteraemia is 10 days.

The routine replacement of catheters in patients with no signs of infection at the catheter site or in haemodynamically stable patients with signs of sepsis, in which the source has not been determined, is not recommended. As mentioned earlier, a large proportion of catheter tips cultured are sterile and removal may not justify the risk of mechanical complication with recannulation, especially in patients with limited venous access.

**Factors related to catheter maintenance.**

Contamination of catheters due to poor maintenance with regard to suboptimal dressings and catheter site skin care leads to increased local skin flora and subsequent catheter contamination. Unnecessary three way taps and multiple connection ports also provide an environment for organism colonisation, especially if these access points are not maintained appropriately.\(^\text{[9]}\)

**Factors related to catheter use.**

Infusion of high lipid content infusate, like total parenteral nutrition and propofol infusions for sedation, and administration of blood products is associated with increased colonisation of catheters. These products provide a medium conducive to organism proliferation and subsequent catheter contamination. Administration of antibiotics through the catheter does not decrease the risk of catheter colonisation.\(^\text{[9]}\)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR-BSI (n = 66) [%]</td>
<td>No CR-BSI (n = 2035) [%]</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>56.9 (16.2)</td>
<td>59.2 (16.4)</td>
</tr>
<tr>
<td>APACHE II, mean (SD)</td>
<td>13.2 (6)</td>
<td>14.5 (7.1)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>50 (75.8)</td>
<td>1,343 (66)</td>
</tr>
<tr>
<td>Type of patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>31 (46.9)</td>
<td>997 (49)</td>
</tr>
<tr>
<td>Medical</td>
<td>20 (30.4)</td>
<td>585 (28.7)</td>
</tr>
<tr>
<td>Others</td>
<td>15 (22.7)</td>
<td>453 (22.3)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13 (19.7)</td>
<td>402 (19.8)</td>
</tr>
<tr>
<td>COPD</td>
<td>5 (7.6)</td>
<td>315 (15.5)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>5 (7.6)</td>
<td>142 (7)</td>
</tr>
<tr>
<td>ESRD</td>
<td>1 (1.5)</td>
<td>59 (2.9)</td>
</tr>
<tr>
<td>CHF</td>
<td>9 (13.6)</td>
<td>264 (13)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>2 (3)</td>
<td>154 (7.6)</td>
</tr>
<tr>
<td>Cancer</td>
<td>7 (10.6)</td>
<td>360 (17.7)</td>
</tr>
<tr>
<td>Place of catheter insertion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jugular vein</td>
<td>17 (25.8)</td>
<td>609 (29.9)</td>
</tr>
<tr>
<td>Subclavian vein</td>
<td>26 (39.4)</td>
<td>559 (27.5)</td>
</tr>
<tr>
<td>Femoral vein</td>
<td>18 (27.3)</td>
<td>369 (18.1)</td>
</tr>
<tr>
<td>PICVC</td>
<td>5 (7.6)</td>
<td>498 (24.5)</td>
</tr>
<tr>
<td>Type of catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PICVC</td>
<td>5 (7.6)</td>
<td>498 (24.5)</td>
</tr>
<tr>
<td>Conventional CVC</td>
<td>61 (92.4)</td>
<td>1,537 (75.5)</td>
</tr>
<tr>
<td>Catheter insertion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change over a guidewire</td>
<td>11 (16.7)</td>
<td>65 (3.2)</td>
</tr>
<tr>
<td>Insertion out of the ICU</td>
<td>17 (25.7)</td>
<td>624 (30.6)</td>
</tr>
<tr>
<td>Time of placement (night)</td>
<td>15 (22.7)</td>
<td>382 (16.1)</td>
</tr>
<tr>
<td>Very difficult insertion</td>
<td>4 (6)</td>
<td>134 (6.6)</td>
</tr>
<tr>
<td>Insertion by a staff member</td>
<td>28 (46.7)</td>
<td>572 (29.6)</td>
</tr>
<tr>
<td>Tracheotomy</td>
<td>13 (19.7)</td>
<td>160 (9.7)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>48 (72.7)</td>
<td>1,201 (59)</td>
</tr>
<tr>
<td>Antibiotic administration</td>
<td>49 (81.7)</td>
<td>1,343 (71.5)</td>
</tr>
<tr>
<td>Administration of a glycopeptide</td>
<td>10 (15.2)</td>
<td>235 (11.5)</td>
</tr>
<tr>
<td>Number of lumens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-lumen</td>
<td>7 (10.6)</td>
<td>405 (19.9)</td>
</tr>
<tr>
<td>Double-lumen</td>
<td>19 (28.3)</td>
<td>618 (30.4)</td>
</tr>
<tr>
<td>Triple-lumen</td>
<td>40 (57.6)</td>
<td>1,012 (49.7)</td>
</tr>
<tr>
<td>Material polyurethane</td>
<td>65 (98.5)</td>
<td>1,994 (97)</td>
</tr>
<tr>
<td>Antiseptic</td>
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<tr>
<td>Chlorhexidine</td>
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<td>1,796 (88.3)</td>
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<tr>
<td>Povidone–iodine</td>
<td>65 (98.5)</td>
<td>1,953 (96)</td>
</tr>
<tr>
<td>Use of three-way stopock</td>
<td>29 (43.9)</td>
<td>1,131 (55.6)</td>
</tr>
<tr>
<td>Use to measure CVP</td>
<td>32 (48.5)</td>
<td>952 (46.7)</td>
</tr>
<tr>
<td>Concomitant infection</td>
<td>11 (8–16)</td>
<td>8 (5–12)</td>
</tr>
<tr>
<td>Catheter use for administration of TPN</td>
<td>19 (28.8)</td>
<td>349 (17.1)</td>
</tr>
<tr>
<td>Propofol</td>
<td>22 (33.3)</td>
<td>464 (22.8)</td>
</tr>
<tr>
<td>Hemoderivatives</td>
<td>13 (19.7)</td>
<td>313 (15.4)</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>54 (81.8)</td>
<td>1,493 (73.4)</td>
</tr>
</tbody>
</table>
Factors related to hospital resources.

Financial constraints have led to a decrease in the number of nursing staff employed by hospitals.

This has resulted in an increase in the number of ‘float’ or ‘pool’ nurses. A float nurse is one who doesn’t work exclusively in a unit but is placed in a particular unit to fill in due to staff shortages. They are generally not familiar with the unit’s policies related to catheter maintenance, leading to contamination of the catheters with subsequent infection.

**Effect of float nurses on the risk of central venous catheter associate bloodstream infection.** \(^{[18]}\)

Due to staff shortages, the patient to nurse ratio has also increased, with one nurse caring for multiple patients. This places time constraints on the nursing staff preventing them from caring for catheters properly and poor hand hygiene with cross contamination between patients. Fridkin et al \(^{[19]}\) found that the number of CRBSI correlated with patient/nurse ratios.
Relationship between Patient/Nurse ratio and the number of CVC-BSI. [19]
GUIDELINES FOR THE PREVENTION OF CATHETER RELATED BLOODSTREAM INFECTION

Prior to Catheter Insertion

**Education, training and staffing.** [3, 18, 19, 20, 21]

Health care workers must be educated about the indications for intravascular catheter insertion, proper procedure for insertion and maintenance and appropriate infection control measures to prevent CRBSI. Education should have theoretical and practical components. Knowledge and adherence to guidelines must be assessed and reinforced regularly. Only trained personnel should insert and maintain intravascular catheters. Intensive care units should have adequate numbers of permanent nursing staff.

**Equipment and checklists.**

There should be a trolley equipped for vessel cannulation containing: skin antiseptics, masks, caps, sterile gowns, sterile and non-sterile gloves, sterile instruments, drapes, intravascular devices and accessories, dressing, etc. A checklist to ensure that an aseptic technique is maintained should be utilised and nurses must be empowered to intervene if the operator doesn’t adhere.

**Systemic antibiotic prophylaxis.** [3, 22]

Administration of prophylactic antibiotics does not decrease the risk of CRBSI. It is associated with complications such as side effects, toxicity and possible organism antimicrobial resistance.

**Antibiotic or antiseptic ointments.** [3]

Topical antibiotics and antiseptics may decrease the risk of infection in patients with haemodialysis catheters. If the ointment is compatible with the catheter, it must be applied to the insertion site after insertion and after each dialysis session. It has not been shown to be beneficial in other patient populations. Topical antibiotics may increase the rate of colonisation with fungi and antibiotic resistance has been described.
At Catheter Insertion

Selection of catheters and site of insertion. [3]

Peripheral and midline catheters: In adults, use the upper extremities for catheter insertion and replace lower extremity catheters as soon as possible. In children, catheters may be inserted in any site. If the duration of therapy is expected to exceed 6 days, insert a midline or peripherally inserted central catheter (PICC).

Central venous catheters (CVC): The site and method of insertion must be selected after weighing the risk of infection and mechanical complications, and should take patient factors and operator experience into account. Choose a CVC with the least number of lumens necessary. If adherence to aseptic technique can’t be guaranteed, the catheter should be replaced within 48 hours. The need for the catheter must be reviewed daily to allow for prompt removal of unnecessary catheters.

Type of catheter. [3, 13, 14]

Teflon® catheters should be used rather than PVC. Antimicrobial and antiseptic impregnated catheters should only be used in patients whose catheter is likely to be in situ for more than 5 days and, if after implementation of a comprehensive strategy (education of personnel, maximal sterile barrier technique, >0.5% chlorhexidine skin antiseptic) to prevent CRBSI, the rate of CRBSI is not decreasing.

Hand hygiene and aseptic technique. [3, 13]

Hand hygiene procedures, i.e. hand washing with conventional soap or alcohol based hand rubs, must be performed before manipulating the catheter or the catheter insertion site in any way and prior to inserting a catheter. Sterile gloves should be worn for insertion of arterial, midline and central venous catheters and when changing the dressing on a catheter. Use new sterile gloves before handling the new catheter when guide wire exchanges are performed. Non sterile gloves may be used for peripheral venous catheters if the access site is not touched after application of skin antiseptic.

Maximum sterile barrier precautions. [3, 13]

This entails the use of a cap, mask, sterile gown, sterile gloves and a sterile full body drape for the insertion of CVCs, PICCs and guide wire exchanges.
Skin preparation. [3]

The skin at the insertion site and surrounding areas must be cleaned with a >0.5% chlorhexidine preparation and the site must dry according to the manufacturer's recommendations prior to cannulation. If chlorhexidine is contraindicated, an iodophor, tincture of iodine or 70% alcohol may be used as an alternative.

Catheter securement devices. [3]

The catheter must be stabilised to decrease the risk of phlebitis, catheter migration and displacement. Sutureless securement devices avoid disruption of the skin at the insertion site and decreases risk of colonisation. It also mitigates the risk of needlestick injury to the health care provider.

After Catheter Insertion

Catheter site dressing regimes. [3]

Use sterile, transparent semipermeable dressing with or without sterile gauze to cover the catheter site.

If the patient is sweating or the site is bleeding or oozing, use a gauze dressing until this resolves. Replace the dressing if it becomes damp, loosened or soiled. Ensure that the catheter and catheter site are not submerged in water and that they are protected with an impermeable dressing during bathing.

Peripheral venous catheters: Transparent dressings can safely be left on for the duration that the catheter is in situ, unless the dressing becomes loosened or soiled.

For short term CVCs and arterial catheters: Replace gauze dressings every 2 day and transparent dressings every 7 days, except in paediatric patients where the risk of dislodging the catheter may be more than the risk of infection.

For tunnelled and implanted CVCs: The transparent dressing must be changed every 7 days until the insertion site has healed.

Chlorhexidine impregnated sponge dressings may be used in patients more than two months old if the rate of CRBSI is still high despite a comprehensive prevention strategy.
Patient cleansing. [3]

Use a 2% chlorhexidine soap wash for daily skin cleansing. This reduces the load of skin flora and decreases risk of colonisation and infection.

Antibiotic or antimicrobial lock prophylaxis. [3]

Catheter lock is a technique by which an antimicrobial solution is used to fill a catheter lumen and then allowed to dwell for a period of time while the catheter is idle. A variety of antibiotics and antiseptics can be used, depending on the spectrum of organisms targeted. The amount used is the amount it takes to flush the catheter, which is usually 1-2ml.

Many studies, mostly in patients on haemodialysis and oncology patients, have been done. Although most of the studies indicate a beneficial effect of the antimicrobial flush or lock solution in terms of prevention of CRBSI, this must be balanced by the potential for side effects, toxicity, allergic reactions, or emergence of resistance associated with the antimicrobial agent. The wide variety of compounds used, the heterogeneity of the patient populations studied, and limitations in the size or design of studies preclude a general recommendation for use. The CDC [3] suggests antibiotic or antimicrobial lock prophylaxis in patients with long term catheters who have a history of repeated CRBSI despite adherence to comprehensive preventative strategies.

Anticoagulation. [3]

The use of anticoagulants routinely is not recommended. The theory behind this intervention is that it decreases catheter related thrombosis, thus decreasing organism adherence and colonisation.

Studies done do show that the infection rate is decreased in patients receiving a heparin infusion through the catheter and in patients with a trisodium citrate catheter lock; however there is uncertainty around whether it is the anticoagulant properties or the antimicrobial properties of the preservative or substance that confers any protection. The risk of side effects, like bleeding and heparin induce thrombocytopenia and toxicity outweighs the benefit of a reduction of infection.

Catheter removal. [3]

The need for the catheter must be assessed daily and the catheter should be removed if it is no longer required. The catheter must be removed immediately if there are any signs of phlebitis or local infection. Patients must be encouraged to report any changes in their catheter site or new discomfort around the catheter.
Replacement of Catheters

Peripheral and midline catheters. [3]

Peripheral venous catheters should not be changed more frequently than every 72-94 hours in adults. In children, peripheral catheters should be changed only when needed, due to difficulty in venous access. Midline catheters should be replaced when needed.

Central venous catheters including PICCs and haemodialysis catheters. [3, 9]

CVC should not be replaced routinely to prevent CRBSI. Don’t remove CVC on the basis of fever alone, CRBSI is a diagnosis of exclusion of other sites of infection. Guide wire changes should not be used routinely and may only be used, in conjunction with an aseptic technique, to replace malfunctioning non tunnelled CVC with no suspected infection. The risk of infection must be weighed against the risk of mechanical complications and patient related factors when deciding on catheter replacement.

Umbilical catheters. [3]

Umbilical artery and vein catheters that have signs of CRBSI, lower limb ischemia or thrombosis should be removed immediately and not reinserted. The umbilical insertion site should be cleaned with any antiseptic agent except tincture of iodine to prevent any adverse effect on the neonate’s thyroid gland. Topical antibiotics should not be used as it increases fungal infections and emergence of antimicrobial resistance. Low dose heparin (0.25-1.0 U/ml) infusion should run continuously. If managed aseptically, umbilical artery catheters should be removed after 5 days and umbilical vein catheters should be removed after 14 days. If there is no other indication for removal, malfunctioning catheter may be replaced if it is less that 5 or 14 days in situ for umbilical artery and vein catheters respectively.

Arterial Catheters [3]

In adults, the radial, brachial and dorsalis pedis arteries are preferred over femoral and axillary sites to prevent infection. The brachial artery should not be used in children. Maximum sterile precautions must be taken. Catheters must be removed as soon as they are not needed. Routine replacement of arterial catheters is not recommended to prevent CRBSI. Disposable transducer sets are preferred over reusable ones and should be changed every 96 hours along with the tubing, flush system and flush fluid. All components of the system must be kept closed and sterile. Stopcocks must be cleaned with antiseptic prior to any manipulations. No dextrose containing solutions or TPN must be given through the arterial catheter. Reusable transducers must be sterilised according to the manufacturer's instruction.
Accessories [3]

Administration sets.

Administration sets that are in continuous use and not used for the infusion of blood products and fat emulsions should be replaced no more frequently than after 96 hours but at least every 7 days.

Tubing used for the administration of blood products or fat emulsions should be changed every 24 hours.

Tubing used to infuse propofol should be changed every 6-12 hours, when the vial is changed or according to manufacturer’s instruction.

Needleless intravascular catheter systems.

In an attempt to reduce needlestick injuries, needleless infusion systems were developed. Stopcocks and needleless connector ports represent a potential portal of entry for organisms into the intravascular catheter. Needleless devices must be changed every 72 hours and when the administration set is changed. Minimize leaks in the system by ensuring all components are compatible. Minimize contamination by scrubbing access ports with antiseptics prior to manipulation and access the ports with sterile devices only. When needleless systems are used, a split septum valve may be preferred over mechanical valves.

Performance Improvement [3]

Each hospital should have quality improvement programmes based on evidence based recommendations. Continuous reinforcement of these measures and ongoing surveillance to determine compliance and impact of the intervention should be carried out.

CARE BUNDELS [2, 3, 23]

The concept of care bundles has generated much interest in recent years. In conjunction with other national and scientific groups, the Institute for Healthcare Improvement (IHI) in the United States promoted ‘care bundles’ as part of an effort to improve patient safety.

A bundle is defined as ‘a group of evidence based interventions that, when implemented together, results in better outcomes than when implemented individually’.
The IHI Central Line bundle consists of five interventions:

1. Hand hygiene
2. Maximum barrier protection upon catheter insertion
3. Chlorhexidine skin antisepsis
4. Optimal catheter site selection with avoidance of the femoral vein for central venous access in adults
5. Daily review of catheter necessity with prompt removal of unnecessary catheters

Rate of CRBSI pre- and post-implementation of care bundles. [2]

<table>
<thead>
<tr>
<th>Study</th>
<th>Site</th>
<th>IHI Bundle?</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berriel-Cass et al (13)</td>
<td>Single center</td>
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<td>9.6</td>
<td>3.0</td>
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<tr>
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</tr>
<tr>
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<td>3.1</td>
</tr>
<tr>
<td>Ronello et al (16)</td>
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<td>2.7</td>
</tr>
<tr>
<td>Costello et al (17)</td>
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<td>2.3</td>
</tr>
<tr>
<td>Galpern et al (18)</td>
<td>Single center</td>
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<td>0.9</td>
</tr>
<tr>
<td>Venkatram et al (19)</td>
<td>Single MICU</td>
<td>Yes + a,b,c,d</td>
<td>10.8</td>
<td>1.7</td>
</tr>
</tbody>
</table>

CRBSI, catheter-related bloodstream infection; ICU, intensive care unit; CICU, cardiac ICU; MICU, medical ICU; a, catheter checklist; b, central venous line insertion cart; c, sterile dressing; d, access/maintenance bundles.

This relative simple collection of interventions has been lauded for having the ability to reduce the CRBSI rates to zero.

Although it seems that bundles reduce infection rates and are likely to stay, the temptation to expand them into more complicated systems should be resisted, as the strength of the bundle arises from its simplicity, consistency and the fact that each component is evidence based. Adding additional components may be associated with decreased adherence to the bundle and no decrease in CRBSI.

A cross sectional study [23] looking at the implementation and compliance of policies in ICUs in the United States showed that there is a wide variability between bundle compliance and infection rates. It was found that instituting bundle policies is becoming common, but only 38% of those that implement care bundles report full compliance.
This is significant as they found that there is no relationship between simply having a bundle policy in place and lower infection rates. It was also found that monitoring the bundle elements and having moderate compliance is not enough to lower infection rates. Central line associated infection rates only decrease when an ICU has a bundle policy, monitors compliance of the bundle elements and has 95% compliance to the bundle policy.

This highlights the importance of monitoring and reinforcement of adherence to bundle policies.

CONCLUSION

The last decade has seen enormous strides in the prevention of CRBSI. Interventions both complex (anti-infective catheters, antimicrobial lock solutions) and fairly simple (bundles and their components) have both contributed to reports of markedly reduced rates of infection. These and other measures are needed urgently, particularly in light of increasing antimicrobial resistance that makes treatment of such infections increasingly difficult.

The old adage that “an ounce of prevention is worth a pound of cure” certainly applies to CRBSIs.
REFERENCES


10. GE Ramos, AN Bolgiani, O Patin. Catheter Infection Risk Related to the Distance Between Insertion Site and Burned Area. Journal of Burn Care and Rehabilitation 2002

11. JC Lucet, L Bouadma, JR Zahar. Infectious Risk Associated with Arterial Catheters Compared with Central Venous Catheters. Critical Care Medicine 2010


15 C Yeung, J May, R Hughes. Infection rate for single lumen versus triple lumen subclavian catheters. Infection Control and Hospital Epidemiology 1988


19 SK Fridkin, SM Per, TH Williamson. The role of understaffing in central venous catheter-associated bloodstream infections. Infection Control Hospital Epidemiology 1996


