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SPECIAL FEATURE

Management of Catheter-related Bloodstream Infections

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Dr. Thompson reports no financial relationships relevant to this field of study.

Since the 1929 introduction of one of the first techniques of vascular cannulation by German physician and physiologist Werner Forssmann, who later went on to share the 1956 Nobel Prize in Medicine,[1] the use of vascular catheters has exploded to the point that U.S. hospitals and clinics purchase more than 150 million intravascular devices each year.[2] Thus, catheter-related bloodstream infections (CRBSIs) remain one of the more common nosocomial infections today, with an estimated 250,000 CRBSIs occurring in the United States annually, of which approximately 80,000 are associated with an ICU stay.[3-5] This is a costly complication of healthcare that also is associated with a significant increase in morbidity and length of stay for patients. The practices used to prevent and treat CRBSIs have evolved dramatically over the years. The science behind current practices has reduced the CRBSI rate by 50% between 2008 and 2014.[6] However, the rate of infection is far from zero,[7] and rates remain significantly different between states, suggesting that there is room for improvement.

DIAGNOSIS

CRBSI should be suspected in the setting of fevers and chills, which are sensitive but not specific. Other sources of infection besides line infection should be sought. The more serious the symptoms and exam findings (e.g., inflammation or purulence at the insertion site, mental status changes, hemodynamic instability), the more specific but less sensitive those findings. The decision to remove a catheter before a definitive diagnosis of CRBSI depends on: the clinician's index of suspicion for line infection rather than another source of fever or infection, how dependent the patient is on the particular line in question, and how unstable the patient is because of the infection.

The definition of CRBSI varies dramatically from study to study,[8] but the more commonly accepted

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definitions come from the CDC[9] and the Infectious Diseases Society of America (IDSA).[2] The CDC definition for central line-associated bloodstream infection (CLABSI) requires a single positive blood culture for an organism not commonly present on the skin or more than two blood cultures for an organism commonly present on the skin, including but not limited to diphtheroids (*Corynebacterium* spp. not *C. diphtheria*), *Bacillus* spp. (not *B. anthracis*), *Propionibacterium* spp., coagulase-negative staphylococci (including *Staphylococcus epidermidis*), viridans group streptococci, *Aerococcus* spp., *Micrococcus* spp., and *Rhodococcus* spp.[10] Additionally, the CDC definition also requires that the central line has been in place within 48 hours before the onset of infection and that the infection is not related to another source in the patient. In those with two or more cultures positive for common skin organisms, the patient also should exhibit at least one of the following signs or symptoms: temperature > 38.0° C, chills, and hypotension.

The IDSA definition of CRBSI requires:
- isolation of the same pathogen from a quantitative blood culture from the central line and from a peripheral vein, with the colony count in the central line at least three-fold higher than that from the peripheral vein; or
- isolation of the same pathogen from the peripheral vein and from quantitative culture of the catheter tip (> 15 colony forming units [CFU]); or
- isolation of the same pathogen from the central line and peripheral vein with a shorter time to positive culture (more than two hours) in the central line using differential time to positivity (DTP) techniques.

Many hospital labs are not equipped with the proper technology to perform quantitative blood cultures, but most can take advantage of the cheaper DTP technology. Quantitative catheter tip cultures are considered positive for colonization with:
- growth of > 15 CFU from a 5 cm segment of the catheter (roll-plate technique); or
- growth of > 102 CFU from a catheter by quantitative (sonication) broth culture technique.

It is also important to stress that catheter tip cultures are recommended only if the catheter is removed for suspicion of CRBSI and not when the catheter is removed routinely.

Culture techniques are outlined by the CDC[9] and IDSA[2] and are crucial to making an accurate diagnosis. A positive culture from the central line and the peripheral vein makes the diagnosis much more definitive. The isolated positive peripheral vein culture is more predictive of CRBSI than is the isolated positive central line blood culture. A positive culture from the catheter with a negative peripheral vein culture is much more likely to be due to contamination than true line infection.[11] On the other hand, a negative culture from both the catheter and peripheral vein carries a good negative predictive value for catheter infection, especially if the patient is off antibiotics. Although there are limited data to support the practice, when a peripheral vein culture is not possible, many will recommend gathering cultures from two different lumens of the central line *and* with two cultures separated in time from each of the lumens. Proper labeling of the source of the cultures is important to confirm the infection.

Tunnel infection is suggested by tenderness or erythema over the subcutaneous tract of a tunneled catheter extending beyond the exit site by > 2 cm and generally requires line removal. On the other hand, inflammation < 2 cm beyond the exit site is suggestive of an exit site infection, which often can be managed more conservatively with topical and potentially IV antimicrobial agents, along with close monitoring.

TREATMENT

Besides considering antibiotic coverage, treatment of CRBSI consists of catheter management, with options that include removal, exchange, or salvage of the catheter. The decision to remove the catheter is based on the certainty of catheter infection, stability of the patient, need for central venous access, ease of replacing

the catheter, and the particular organism growing in cultures. Once CRBSI is confirmed, all non-tunneled catheters should be removed. Even tunneled catheters require removal for the following: hemodynamic instability suggesting sepsis, any evidence of endocarditis or other metastatic infection, persistent bacteremia or symptoms of infection after 72 hours of appropriate antibiotic therapy, and also suppurative thrombophlebitis.

Certain bacteria also preclude any consideration of salvage therapy. *Pseudomonas aeruginosa*, *Staphylococcus aureus*, fungi, mycobacteria and low-virulence but difficult-to-eradicate-bacteria (*Micrococcus* spp., *Bacillus* spp., *Cutibacterium* spp., etc.) necessitate catheter removal. Growth of gram-negative bacilli or enterococci also requires removal of short-term catheters (in place for < 14 days).

In the absence of the above conditions and organisms, salvage therapy with IV antibiotics and antibiotic lock therapy (ALT) can be considered for long-term catheters, including tunneled hemodialysis catheters, in patients with limited vascular access and uncomplicated CRBSI.[2,12] Salvage therapy can be considered for coagulase-negative *Staphylococcus* infection, but patients still will be at high risk of recurrent infection.[13] Salvage therapy consists of systemic antibiotics coupled with antimicrobial lock therapy. ALT is ineffective against extraluminal infections as well as any infection due to *S. aureus*, *P. aeruginosa*, *Candida*, or drug-resistant, gram-negative bacilli.

Generally, ALT occurs with an antibiotic to which the organism is susceptible, at high concentration, and often with heparin to prevent occlusion of the catheter. Justo and Bookstaver provided a table of suggested antibiotic concentrations and heparin doses.[14] It is important that pharmacy and nursing coordinate care closely and that lumens with the lock therapy are labeled clearly. Persistent symptoms after 36 hours or positive cultures repeated at 72 hours require catheter removal.

Guidewire exchange is supported only by small, uncontrolled studies and should be considered only when a catheter requires removal and the risk of mechanical or bleeding complications with placement of a new catheter is high. The risk of recurrent infection with guidewire exchange may be lower when an antimicrobial surface-treated catheter is used,[15] but further studies will be required to confirm this. In the dialysis-dependent patient with poor venous access, exchange over a guidewire could be considered when symptoms of infection resolve within two to three days of IV antibiotic therapy through the infected catheter, when the causative microorganism is not one of the resistant organisms listed above, and when there is no evidence of metastatic infection.[12]

Empiric antimicrobial therapy is recommended when there is a high index of suspicion for CRBSI — even before cultures return positive. Because of the high rate of gram-positive infections, empiric therapy almost always includes vancomycin or, when resistance is suspected, daptomycin or other agents against gram-positive organisms. Linezolid generally is not considered because it is bacteriostatic rather than bactericidal and it produces problematic side effects. Questions related to lower survival rates compared to vancomycin have led the FDA to issue a warning against use of linezolid for the empiric treatment of CRBSI.[16] Gram-negative coverage also is included in the setting of sepsis, neutropenia, and known gram-negative colonization, and when the local incidence of gram-negative infection is high. Coverage against candidemia should be considered in the setting of candidal colonization, a femoral line, transplant patients, those with hematologic malignancies, recent treatment with broad-spectrum antibiotics, or if the patient is receiving parenteral nutrition. Empiric antifungal therapy would include echinocandin or azole agents. For candidemia, fluconazole can be considered for selected patients without azole exposure in the previous three months and in settings in which the risk of *Candida krusei* or *Candida glabrata* infection is very low. Empiric therapy always should be tailored to the specific infection once identification and sensitivities return.

Length of therapy also is dependent on the particular organism and whether any metastatic infection is identified. For uncomplicated *Staphylococcus aureus* infections with confirmed sensitivities, 14 days of vancomycin (for MRSA) or nafcillin/oxacillin usually is recommended. Length of therapy would be extended in the setting of metastatic *S. aureus* infection. With *S. aureus* bacteremia, the risk of endocarditis can be as high as 25-32%; thus, transesophageal echocardiogram (TEE) should be considered five to seven days after onset of bacteremia.[17] The risk for metastatic infection with *S. aureus* increases with community-acquired infection, intravascular devices, immunocompromised state (renal failure, diabetes, dialysis, etc.), valvular abnormality, suppurative thrombophlebitis, and delay in catheter removal.[18]

For coagulase-negative Staphylococcus, five to seven days with catheter removal often is sufficient, although some would consider up to three weeks when endovascular hardware is present. Infection with gram-negative bacilli or with enterococci generally are treated with catheter removal and 10-14

days of antibiotics. The risk of endocarditis is low with *Enterococcus faecium*[19] but much higher with *Enterococcus faecalis*. Thus, TEE should be considered when *E. faecalis* is cultured or with any CRBSI with persistently positive cultures at 72 hours or any other evidence of prolonged infection. Typically, candidemia is treated for 10-14 days after catheter removal and after the first day of negative blood cultures. With any organism, persistently positive blood cultures or any documented metastatic infection usually will require extending the length of therapy.

Conditions that generally do not require antibiotic therapy include phlebitis or thrombosis without other evidence of infection and positive catheter tip culture without signs and symptoms of infection. Depending on the organism cultured, a positive blood culture through the catheter with a negative peripheral vein culture often is due to contamination and may not need to be treated. Catheter removal also may not be necessary with unexplained fever in the hemodynamically stable patient without any endovascular prosthetic material (vascular graft, prosthetic valve, etc.).

PREVENTION

For the sake of patient care and because treatment of CRBSI generally is a very costly and preventable complication that is often not reimbursed by Medicare, resources spent on prevention usually are cost effective. Guidelines for the prevention of CRBSI are well documented[4,12] and will not be reviewed in detail here. Such guidelines have been used to develop protocols for employee education, central line insertion, routine line care, daily chlorhexidine skin cleansing, and accessing the central line in most institutions.

For the clinician, some of the more important points to remember include choice of location of the central line. Parienti et al[7] compared risks of complications at the subclavian, jugular, and femoral venous sites. They found the risk of bloodstream infection (0.5%, 1.4%, 1.2%, respectively) and symptomatic deep-venous thrombosis (0.5%, 0.9%, 1.4%) were significantly lower in the subclavian location, while the risk of pneumothorax/mechanical complications (2.1%, 1.4%, 0.7%) was higher in the subclavian lines.

Use of ultrasound guidance usually will reduce the number of cannulation attempts and risk of mechanical complications. Hand hygiene, maximal sterile barrier precautions (cap, mask, sterile gown, sterile gloves, sterile full body drape), and the use of > 0.5% chlorhexidine skin preparation are some of the central line insertion techniques most important for preventing central line infection. When use of a strict aseptic technique cannot be ensured as in emergent lines, the catheter should be replaced as soon as possible. Dressing techniques are well described and include replacing the dressing when damp, loose, or visibly soiled. Topical antibiotic ointment should not be used at insertion sites except for dialysis catheters because of the potential to promote infection with fungi or antimicrobial-resistant organisms. It has been shown that the risk of dialysis catheter infection decreases with the use of antibiotic or povidone-iodine ointment to catheter exit sites.[12] Central lines also should be removed when no longer necessary.

The benefits of antimicrobial-impregnated catheters (chlorhexidine-silver sulfadiazine, minocycline-rifampin) and silver-impregnated catheters remain unclear.[2,20,21] While many centers use these catheters routinely, others favor their use only when a center's CRBSI rate is higher than national surveillance rates despite adherence to other standard prevention protocols.[4]

In short, CRBSI is a common, costly, and often preventable cause of morbidity and extended length of stay in the ICU. Prevention, diagnosis, and treatment guidelines are well documented and, when strictly followed, can significantly improve outcomes in patients. ■

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ABSTRACT & COMMENTARY

Real-time Tracking of Influenza-related ICU Use

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Dr. Benthin reports no financial relationships relevant to this field of study.

SYNOPSIS: Surrogate markers of influenza severity, specifically trends in ICU use, were collected and revealed differences from current influenza reporting.

SOURCE: Baker AW, Edmond MB, Herwaldt LA, et al. Real-time surveillance of influenza morbidity: Tracking intensive care unit resource utilization. *Ann Am Thorac Soc* 2017;14:1810-1817.

The annual seasonal severity of influenza varies and results in yearly fluctuation of healthcare system use, including ICU resources. Current real-time reporting of influenza morbidity and mortality within the United States is limited to hospitalization and influenza plus pneumonia composite mortality as presented by the CDC's weekly update.[1] These data do not predict the need of hospital resources precisely, including ICU beds, ventilators, or use of extracorporeal membrane oxygenation (ECMO). The CDC's online Influenza Hospitalization Surveillance Network database provides a more comprehensive description of severity, including ICU use (but only retrospectively).

The aim of this study was to determine if a surveillance system using sentinel hospitals within the United States that serially recorded days of ICU admission, mechanical ventilation, and ECMO use on a weekly basis could provide an accurate and opportune description of influenza severity and associated resource use. Baker et al developed a pilot study to collect data retrospectively from a 36-week period of the 2013-14 influenza season at three tertiary care hospitals, which included 2,408 beds in three separate states. Subjects included were all patients requiring inpatient admission diagnosed with influenza based on a positive respiratory sample polymerase chain reaction (PCR) or who had received an influenza-related diagnosis code (ICD-9).

The weekly number of influenza admissions, patients started on mechanical ventilation, or ECMO were recorded. The days accrued in the ICU, on mechanical ventilation, or on ECMO also were tracked. Data from Hospital A were extracted

through electronic health record (EHR) queries, whereas manual chart review was completed at Hospitals B and C. Overall, 431 patients were identified to be hospitalized with influenza from Aug. 4, 2013, through April 12, 2014. Influenza admissions represented 0.6% of the total 76,968 admissions, and 81% of the patients were adults (> 18 years of age). The majority were identified by positive PCR (83%).

Twenty percent of patients required mechanical ventilation, averaging 12.5 days on a ventilator. Four percent of patients required ECMO, averaging 13.5 days. Deaths varied between hospitals (2.8% at Hospital B and 12.5% at Hospital C).

Weekly trends in admissions and ICU use varied between hospitals, with Hospital A demonstrating an earlier peak of resource use, which coincided with hospitalization and death. However, Hospitals B and C showed a later peak of hospitalization, which was followed by later peaks in ICU resource use. The combined network influenza hospitalization rate declined rapidly following its peak; however, rates of ICU, mechanical ventilation, and ECMO use remained elevated.

■ COMMENTARY

The findings of this study demonstrate that trending weekly rates of influenza-specific ICU resource use, including beds, mechanical ventilation, and ECMO, is feasible, and suggests the possibility that multicenter surveillance of influenza outbreaks in this manner could add to existing real-time severity updates. Tracking trends in ICU beds and mechanical ventilation use may be superior to death given the relatively low rate of the latter endpoint. As demonstrated in the data collection of this study, advances in EHR allow for robust data queries within health systems. These may require advanced coding techniques initially, but subsequent queries may be substantially more efficient. We know that there are limitations in our current traditional healthcare-based systems for reporting influenza activity, and internet-based data sources such as Google have been used to produce activity estimates ahead of these systems.[2,3] As seen in this study, regional differences of peak influenza rates would be expected to produce similar differences in ICU use. In fact, there are efforts underway to develop accurate local (city or regional) influenza monitoring and forecasts based on these advances.[4]

Influenza continues to be a major challenge affecting health systems, requiring periods when ICU resources are in higher demand. These outbreaks vary depending on the timing and severity of each season, the virulence of circulating strains, and the populations affected. Given these points, the real-time monitoring and reporting of ICU use may contribute significant knowledge, which would aid in planning for anticipated resource need. ■

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ABSTRACT & COMMENTARY

Routine Chest Radiographs After Ultrasound-guided Central Line Placement May Be Unnecessary

By Samuel Nadler, MD, PhD

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Dr. Nadler reports no financial relationships relevant to this field of study.

SYNOPSIS: Catheter misplacement and pneumothorax after routine ultrasound-guided catheter placement are rare, and routine post-procedural chest radiographs may not be cost-effective.

SOURCE: Chui J, Saeed R, Jakobowski L, et al. Is routine chest X-ray after ultrasound-guided central venous catheter insertion choosing wisely? A population-based retrospective study of 6875 patients. *Chest* 2018 Feb 28. pii: S0012-3692(18)30341-6. doi: 10.1016/j.chest.2018.02.017. [Epub ahead of print].

Chest radiographs are performed routinely after central venous catheterization to confirm appropriate placement and evaluate for procedural complications such as pneumothorax. With the increased use of ultrasound-guided placement, the procedural risks have decreased, raising concerns about whether routine radiographs remain cost-effective.

Chui et al conducted a retrospective analysis of all adult patients in an academic center who received a central line in the operating room. Patients were excluded if they underwent cardiothoracic surgery, received a femoral line, or did not undergo a post-procedural chest radiograph.

The authors identified a cohort of 6,875 patients and determined the incidence of pneumothorax and catheter misplacement. The most common site of placement was the right internal jugular vein (85%), followed by the left internal jugular (6%), and the subclavian veins (4% each side). A short (15 cm) central venous line was used most commonly (99%), with few pulmonary artery catheters (< 1%) or large-bore central venous catheters placements (< 1%).

The overall rate of pneumothorax was 0.33%, with 0.12% of patients requiring chest tube placement. The strongest risk factor for pneumothorax with multivariate analysis was a left subclavian site (odds ratio, 6.58; $P < 0.001$). Catheter misplacement occurred in 1.91% of procedures, most commonly with coiling in superior vena cava/subclavian/innominate vein (53%), most of which did not require repeat chest radiograph for repositioning (82%). Use of a site other than the right internal jugular vein was associated with an increased risk of misplacement.

Assuming the cost of a chest radiograph of $115-$200 per film, the cost to diagnose one pneumothorax was $34,375-$59,783, while the cost to diagnose a misplaced catheter was $6,043-$10,496. When considering only post-procedural complications requiring interventions, the number needed to test for pneumothorax was 860 at a cost of $98,828-$171,875 per chest drainage. For catheter misplacement, the number needed to test was 286, with a cost of $32,942-$57,292 per catheter repositioning.

■ COMMENTARY

Chui et al examined the likelihood of complications from central venous catheterization and the costs associated with chest radiographs to screen for these complications. The relatively large number of patients examined is a strength of this study. However, generalizing this study creates a few limitations. First, all the central lines were placed in the operating room with ultrasound guidance under ideal conditions in surgical patients. Complication rates in other settings, such as the ICU or general medical ward, may be higher, and the need for interventions for pneumothorax or catheter misplacement may be greater with prolonged mechanical ventilation and catheter use. Second, a short central catheter (15 cm) was used, which reduces the likelihood of coiling. Third, this was a single institution study, with ultrasound guidance widely available for central line placement.

With these caveats, a few conclusions can be drawn. Catheterization in the right internal jugular vein using ultrasound appears to carry a low complication rate. When pneumothorax or catheter misplacement was noted, most complications did not require additional intervention. Furthermore, other techniques to determine pneumothorax and catheter placement, such as thoracic ultrasound, are available. For pneumothorax specifically, ultrasound may be more sensitive.

In short, the cost of routine chest radiographs that change management is quite high, and routine post-procedural chest radiography may be unnecessary and a poor use of resources. ■

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CME/CE QUESTIONS

1. **Which of the following measures does *not* decrease the risk of central venous catheter-related bloodstream infection?**
   a. Use of the subclavian rather than the internal jugular site for line placement
   b. Topical antibiotic ointment at the insertion site of all central venous catheters
   c. Maximal sterile barrier precautions during catheter placement
   d. Good hand hygiene

2. **In the article by Baker et al, which of the following surrogate markers of influenza severity was *not* included in the real-time surveillance of influenza morbidity?**
   a. ICU days
   b. Mechanical ventilation
   c. ECMO
   d. Renal replacement therapy

3. **In the article by Baker et al, which of the following statements is correct regarding the patient population?**
   a. It represented 6% of total admissions over a 36-week period.
   b. Twenty percent required mechanical ventilation.
   c. One percent required ECMO.
   d. The diagnosis of influenza was made by PCR in 50% of patients.

4. **In the study by Chui et al, routine chest radiographs after central venous line placement:**
   a. detected a high rate of procedural complications, > 10%.
   b. commonly led to additional interventions to correct procedural complications.
   c. showed an overall rate of pneumothorax and catheter misplacement of 0.33% and 1.91%, respectively.
   d. showed minimal cost to detect each complication.

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.