

Update in Nonpulmonary Critical Care

Enhancing the Safety of Critically Ill Patients by Reducing Urinary and Central Venous Catheter-related Infections

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Indwelling urinary and central venous catheters are commonly used in the care of critically ill patients. Though both types of devices provide important clinical benefits, they are also the leading causes of nosocomial infection in the intensive care unit (ICU). Enhancing the safety of critically ill patients requires that critical care specialists be aware of the proven methods for preventing urinary catheter-related and central venous catheter-associated infection. To this end, we provide a concise evidence-based overview of preventive methods for both urinary and central venous catheter-related infection. The objective of this update is to consider the evidence supporting specific preventive methods, devoting more attention to recently evaluated interventions and to interventions that many consider controversial (e.g., silver alloy urinary catheters, antimicrobial central venous catheters). Several recent evidence-based reviews provide additional details about the risk factors, microbiology, and pathophysiology of each infection, and provide a more comprehensive review of all the potential preventive methods (1–3). This review is derived from the evidence report produced by the Evidence-Based Practice Center at the University of California at San Francisco–Stanford University, under contract with the Agency for Healthcare Research and Quality (4, 5).

URINARY CATHETER-RELATED INFECTIONS

Catheter-related urinary tract infection (UTI) is the most common nosocomial infection seen in medical ICUs in the U.S., accounting for 31% of nosocomial infections (6). The daily incidence of bacteriuria in catheterized patients is approximately 3–10% (7). Among patients with bacteriuria, up

to 25% will develop symptoms of local UTI, and about 3% will develop bacteremia (7). Each episode of hospital-acquired symptomatic catheter-related UTI costs an additional US \$676, and each episode of catheter-related nosocomial bacteremia costs a minimum of US \$2,836 (7).

PREVENTIVE MEASURES FOR URINARY CATHETER-RELATED INFECTION

Avoid and/or Curtail Use of Indwelling Catheters

The best strategy to prevent nosocomial UTI is to avoid catheterization. Unfortunately, unjustified and excessively prolonged catheter use is common, even in the critically ill (8). Jain and coworkers found that initial catheter insertion was unjustified in 13% of 135 catheterized patients in a medical ICU; continued catheter use was deemed inappropriate for 41% of catheterized patient-days (8). The most common reason for inappropriate catheter use among these medical ICU patients was for close monitoring of urine output; however, the investigators found that often there was no longer a clinically appropriate indication for close urine output monitoring or that an indwelling catheter was not required for this purpose (8).

Closed Drainage Systems and Use of Aseptic Insertion Techniques

The use of proper insertion and maintenance techniques is paramount. The most important infection control advance in urinary catheter-related infection prevention was the introduction approximately four decades ago of the closed catheter drainage system. Maintenance of a closed system includes the use of sealed urinary catheter junctions. Proper aseptic technique, including aseptic insertion and maintenance of the catheter and drainage bag, remain essential in preventing catheter-related UTI. This is important to remember in critically ill patients when there may be a sense of urgency to insert a urinary catheter.

Use of Antiinfective Urinary Catheters

Antiinfective agents applied to the surface of urinary catheters have generally been shown to be effective in preventing bacteriuria; however, most of the data is derived from hospitalized patients not in an ICU. The most commonly used substance is silver. Although the results reported in eight randomized controlled trials evaluating the silver-coated catheter were mixed, certain types of silver-coated urinary catheters, notably silver alloy catheters, appear to reduce the rate of bacteriuria according to a recent meta-analysis (9). Five studies of silver alloy urinary catheters published after the meta-analysis, most of which focused primarily on bacte-

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riuria, are also instructive. Two of the studies have shown a statistically significant benefit (but with a smaller relative risk [RR] reduction compared with the meta-analysis) of silver alloy catheters (10, 11); both studies included patients in an ICU. However, when Karchmer and colleagues (10) performed subgroup analysis on ICU patients, there was no statistically significant benefit seen in patients given silver alloy catheters (RR, 0.94; 95% confidence interval [CI], 0.64–1.38). One study, which included intensive care and neurosurgical patients, failed to find a significant benefit associated with silver alloy catheters (12), and another study, which only evaluated postoperative urological patients, found a significant benefit of silver alloy catheters in those given the silver alloy catheter for about 5 days but not in those given the new catheter for 14 days (13). Finally, in a before-and-after five-center evaluation that focused entirely on ICU patients, Bologna and coworkers found a significant benefit in the silver alloy catheter group in the unadjusted analyses (37% risk reduction; $p < 0.001$), but not in the adjusted analyses (40% risk reduction; $p = 0.13$) (14).

Given the potential clinical benefits of silver alloy catheter use coupled with the consequences of catheter-related UTI and limited alternative methods of prevention, we recommend silver alloy catheters in those considered at highest risk for infection (e.g., the critically ill or immunocompromised). Of note, the University of Michigan Medical Center is currently using the silver alloy catheter in patients residing in an ICU or on the hematology–oncology floors and evaluating both the clinical and economic consequences of this targeted approach.

Catheters coated with antibacterial substances other than silver have also been evaluated, but to a much lesser extent compared with silver catheters (see Table E1 in the online data supplement). A recent randomized study of men undergoing radical prostatectomy found that patients who received antimicrobial-impregnated catheters coated with minocycline and rifampin had significantly lower rates of gram-positive bacteriuria than the control group subjects who were given standard catheters, but similar rates of gram-negative bacteriuria and candiduria (15). The theoretical risk of developing antimicrobial resistance to minocycline and/or rifampin (two agents occasionally used systemically) will likely limit the use of urinary catheters coated with these substances.

Summary of Preventive Methods against Catheter-related UTI

Urinary catheter-related infection is common, costly, and morbid. Few interventions decrease this important complication. Silver alloy urinary catheters may reduce nosocomial UTI among the critically ill. It is less clear what effect silver alloy urinary catheters will have on such outcomes as urinary catheter-related bacteremia and mortality. At present, using silver alloy catheter in those at highest risk for catheter-related UTI (e.g., the critically ill) seems reasonable. Regardless of which type of urinary catheter is used, two aspects remain critical. First, a urinary collection device should be used only when appropriate and discontinued as soon as catheterization is no longer required. Second, aseptic techniques should be used at all times in both the insertion and management of the catheter, and the drainage system should be manipulated as infrequently as possible.

CENTRAL VENOUS CATHETER-ASSOCIATED INFECTIONS

Central venous catheters (CVCs) inserted for short-term use have become common and important devices in caring for the

critically ill. Although they have important advantages, CVCs are the most common cause of nosocomial bacteremia in the ICU (16). Mermel has recently estimated that each year approximately 80,000 episodes of catheter-related bloodstream infection (CR-BSI) occur in U.S. ICUs, which lead to between 2,400 and 20,000 deaths and cost between US \$296 million and US \$2.3 billion annually (1, 17). Incidence rates of CR-BSI vary substantially depending on the type of ICU. The Centers for Disease Control and Prevention reports an average CR-BSI rate of 2.8 (in cardiothoracic ICUs) to 10 (in burn units) infections per 1,000 catheter-days for all types of ICUs and average rates of 4.1–6.1 infections per 1,000 catheter-days for medical/surgical ICUs (18).

The most common organisms causing catheter-related infections include staphylococci (both coagulase-negative and *Staphylococcus aureus*), enterococci, gram-negative rods, and *Candida* species. Resistance to antimicrobials has increased over the past decade for many of the common pathogens (18). Among ICU isolates, approximately 25% of enterococci are now resistant to vancomycin, 23% of *Pseudomonas aeruginosa* are quinolone resistant, and more than 50% of *S. aureus* isolates are resistant to methicillin (18).

DEFINITION AND EVALUATION OF CR-BSI

A recent evidence-based report provides comprehensive guidelines for the management of suspected and confirmed intravascular catheter-related infections (19). CR-BSI is defined as bacteremia or fungemia in a patient who has an intravascular device and one or more positive blood culture samples obtained from the peripheral vein, clinical manifestations of infection (such as fever, chills, and/or hypotension), and no apparent source for bloodstream infection (other than the CVC). In addition, one of the following should be present: (1) a positive result of semiquantitative (≥ 15 colony forming units [CFU] per catheter segment) or quantitative ($\geq 10^2$ CFU per catheter segment) CVC culture, whereby the same organism is isolated from a CVC segment and a peripheral blood sample; (2) simultaneous quantitative cultures of blood samples with a ratio of not less than 5:1 (CVC versus peripheral); and (3) differential time to positivity (positive blood culture occurs at least 2 hours earlier in the sample from the CVC than in the peripheral blood). Given the difficulty in verifying the diagnosis of CR-BSI, intensivists should ideally work with colleagues from infectious diseases and laboratory medicine to obtain some of the aforementioned technologies in hospital microbiology departments.

When there is evidence of erythema or purulence around a CVC site, the catheter should be removed and a new catheter inserted at a different site. If the patient appears clinically to have CR-BSI in the setting of a clean CVC site, then the evidence-based options are less clear. The infectious risks of changing the CVC over a guidewire must be balanced with the mechanical complications (i.e., pneumothorax, hematoma) of inserting a new catheter at a different site. At our institutions, in the aforementioned setting, the line is changed over a guidewire, and the CVC tip (or a subcutaneous segment) is usually sent for semiquantitative analysis. If the culture of the line segment becomes positive (≥ 15 CFU per catheter segment), the CVC is removed and a catheter is placed with a new puncture at another site. It is also important to note that if a patient continues to have clinical evidence of CR-BSI persisting more than 3 days after removal of the CVC, then an aggressive search should be performed to exclude septic thrombosis or endocarditis.

PREVENTIVE MEASURES FOR CENTRAL VENOUS CATHETER-RELATED INFECTION

There are several important practical issues to be considered in reducing the incidence and severity of CVC-related infection. This section will discuss each of these issues in the context of the best, most recent available controlled clinical trials and provide guidelines based on practical considerations.

Duration of Catheterization

Because of the increased risk of infection with prolonged catheterization, many clinicians attempt to reduce this risk with routine changes of the catheter, either over a guidewire or with a new insertion site. However, the available data do not support this practice. Eyer and coworkers (20) randomized 112 surgical patients receiving a central venous, pulmonary arterial, or systemic arterial catheter for more than 7 days into three groups: (1) weekly catheter change at a new site; (2) weekly guidewire exchange at the same site; or (3) no routine weekly changes. No significant difference was noted in the incidence of local or bacteremic infection (20). Cobb and colleagues randomized 160 patients with central venous or pulmonary arterial catheters to either replacement every 3 days at a new site or over a guidewire, or replacement only when clinically indicated (21). In those with replacement catheters at new sites, the risk of infectious complications was not decreased, and the number of mechanical complications was increased. Those undergoing routine replacement via a guidewire exchange showed a trend toward a higher rate of bloodstream infections compared with those who had catheter replacement only when clinically indicated (21). A recent meta-analysis has confirmed that routine changes of central venous and systemic arterial catheters appear unnecessary (22).

Choice of Insertion Site

The location of CVC placement is an important risk factor for infection likely due to the density of skin flora at the insertion site. A recent randomized trial in eight ICUs in France provided clear evidence that patients given CVCs in the femoral vein had significantly higher rates of catheter-related infection (and thrombotic complications) compared with patients catheterized in the subclavian vein (overall infectious complications—19.8 versus 4.5%, $p < 0.001$; overall thrombotic complications—21.5 versus 1.9%; $p < 0.001$) (23). Though no randomized study has compared the risks of catheterization of the subclavian vein with that of the internal jugular vein, observational studies indicate that central venous and pulmonary arterial catheters inserted in the subclavian vein seem to have a decreased risk of infection compared with those inserted into the internal jugular vein (24); mechanical complications (e.g., bleeding, pneumothorax), however, are more common with subclavian vein catheters than with internal jugular catheters. Thus, whereas the femoral site should generally be avoided due to the high risk for infection, the decision between the subclavian and internal jugular veins should be based on several factors including the risk of infectious and mechanical complications, operator skill and experience, and patient-related factors (e.g., bleeding diathesis).

Use of Maximum Sterile Barriers during Insertion

Strict adherence to proper handwashing and use of proven infection control principles are crucial. A more active measure to prevent infection includes the use of maximum sterile barriers (MSB) during CVC insertion. MSB consist of the use of sterile gloves, long-sleeved gowns, and a full-size drape as well as a nonsterile mask (and often a nonsterile cap) during CVC

insertion. There is moderately strong evidence supporting the use of MSB to decrease the risk of catheter-related infection. A study of 297 patients with pulmonary arterial catheters (94% of the patients were mechanically ventilated) revealed that patients who had the catheter inserted without using MSB were about twice as likely to develop catheter-related infection compared with patients who had catheter placement using MSB (24). A clinical trial of outpatients with cancer (about half of whom were subsequently hospitalized during the study) randomized 176 patients to catheter insertion using MSB and 167 patients to control (use of sterile gloves and sterile small drape) and found that the rates of CR-BSI per 1,000 catheter-days were significantly different (0.5/1000 in control group versus 0.08/1000 in intervention groups; $p = 0.02$) (25). Finally, a recent nonrandomized pre-post observational evaluation, which focused on critically ill medical and surgical patients, by Sherertz and colleagues (26) found that a 1-day course on infection control practices significantly increased MSB use (from 44 to 65%), while significantly decreasing catheter-related infection by 28% (26).

Use of CVC Coated with Antimicrobial Agents

Much recent attention has focused on the use of CVCs coated with antimicrobial agents to reduce the incidence of CR-BSI. Because these catheters are more expensive than standard catheters, pathogenesis, efficacy, and cost-effectiveness need to be considered before widespread implementation.

The microbial pathogenesis of CR-BSI has two major components: (1) extraluminal infection, which occurs primarily via direct migration of cutaneous bacteria to the tip; and (2) intraluminal infection, which usually occurs via spread from bacteria on the catheter hub. Extraluminal infection usually occurs within 1 week after insertion, whereas intraluminal infection commonly occurs in CVCs inserted for longer periods of time.

Several randomized trials have compared chlorhexidine/silver sulfadiazine CVCs (coated only on the external surface) with standard, noncoated CVCs, as has a recent meta-analysis (27). The meta-analysis found that patients given chlorhexidine/silver sulfadiazine catheters had a statistically significant decrease of approximately 40% in the incidence of CR-BSI (27). A recent randomized trial of minocycline/rifampin (impregnated on both surfaces) versus chlorhexidine/silver sulfadiazine catheters, however, found a significant decrease in the incidence of CR-BSI in the group of patients using minocycline/rifampin (0.3 versus 3.4%, $p < 0.002$) (28). Both types of coated catheters had similar efficacy for approximately the first week of catheterization.

A recent formal economic evaluation compared chlorhexidine/silver sulfadiazine catheters with standard catheters, finding that chlorhexidine/silver sulfadiazine catheters lead to both clinical and economic advantages in patients considered high risk for infection (e.g., the critically ill or immunocompromised patients) receiving central venous catheterization for 2–10 days (29). In deciding which antimicrobial catheter to use, it is important note that minocycline and rifampin are substances that are still occasionally used as systemic antimicrobial agents; their use on catheters thus raises the theoretical issue of increased antimicrobial resistance. We, therefore, recommend using the chlorhexidine/silver sulfadiazine catheter in high-risk patients requiring short-term central venous catheterization (e.g., for 2–10 days). Indeed, the University of Michigan Medical Center is currently using the chlorhexidine/silver sulfadiazine catheters in all of its adult ICUs. Finally, a newer chlorhexidine/silver sulfadiazine catheter is now available in which the antiseptic is located on both the internal and

TABLE 1. CHARACTERISTICS AND OUTCOMES OF STUDIES COMPARING CHG AND PI SOLUTIONS FOR VASCULAR CATHETER SITE CARE* (30)

	Antiseptic CHG Solution	Patient Population	Number of Catheters (Number of Patients)		Catheter Duration Mean Number of Days		Outcomes RR (95% CI) CHG versus PI	
			CHG Group	PI Group	CHG Group	PI Group	Catheter Colonization	Catheter-related Bloodstream Infection
Maki and coworkers, 1991	2% aqueous	ICU	214 (214)	227 (227)	5.3	5.3	0.25 (0.10, 0.66)	0.18 (0.02, 1.46)
Sheehan and coworkers, 1993	2% aqueous	ICU	169 (94)	177 (95)	NA	NA	0.22 (0.06, 0.75)	1.05 (0.07, 16.61)
Meffre and coworkers, 1995 [†]	0.5% alcohol 70%	Hospital	568 (568)	549 (549)	1.6	1.6	0.40 (0.18, 0.85)	0.97 (0.20, 4.77)
Mimoz and coworkers, 1996	Biseptine [‡]	ICU	170 (NA)	145 (NA)	4.5	3.9	0.43 (0.22, 0.82)	0.64 (0.15, 2.81)
Cobett and LeBlanc, 1999 [†]	0.5% alcohol 70%	Hospital	83 (83)	161 (161)	1.6	1.7	0.49 (0.31, 0.77)	—
Humar and coworkers, 2000	0.5% alcohol	ICU	193 (193)	181 (181)	5.3	6.3	1.33 (0.87, 2.04)	0.75 (0.20, 2.75)

Definition of abbreviations: CHG = chlorhexidine gluconate; CI = confidence interval; ICU = intensive care unit; NA = not available; PI = povidone iodine; RR = risk ratio.

* All studies used 10% povidone iodine solution.

[†] Additional information was provided by the author.

[‡] Biseptine consists of 0.25% CHG, 0.025% benzalkonium chloride, and 4% benzyl alcohol.

external surfaces; studies comparing this new catheter with the minocycline/rifampin catheter are underway.

Use of Chlorhexidine Gluconate at the CVC Insertion Site

Microbial populations on the skin are routinely suppressed with antiseptic agents before catheter insertion. Povidone iodine (PI) is overwhelmingly the most commonly used agent for this purpose in the U.S. Recently, several studies have compared the efficacy of PI and chlorhexidine gluconate (CHG) solutions in reducing vascular catheter-related infections. The study characteristics and outcomes of the several randomized trials comparing any type of CHG solution with PI solution for vascular catheter site care are shown in Table 1 (30). The majority of the trials reveal that CHG solution results in a significant decrease in catheter colonization and a trend in reducing CR-BSI incidence. Because the lack of significant results in CR-BSI rates may be a result of insufficient statistical power in the individual studies, a formal meta-analysis was recently performed, which indicates that CHG solution reduces the incidence of CR-BSI by approximately 50% (30). Thus, using CHG rather than PI for catheter site care in the ICU appears to be a simple and effective method of reducing CR-BSI.

Use of Heparin with CVC

Because an association has been shown between thrombus formation and catheter-related infection, clinicians usually use heparin given in different forms: (1) as flushes to fill the catheter lumens between use; (2) injected subcutaneously; or (3) bonded on the catheter. A meta-analysis of 12 randomized trials (most of the patient populations of these trials consisted of adult medical and surgical patients) evaluating prophylactic use of heparin in patients using CVCs has shown that prophylactic heparin decreases catheter-related venous thrombosis (RR, 0.43; 95% CI, 0.23–0.78) and bacterial colonization (RR, 0.18; 95% CI, 0.06–0.60) and may decrease CR-BSI (RR, 0.26; 95% CI, 0.07–1.03) (31). Because subcutaneous heparin also offers benefit in reducing venous thromboembolism in certain patient populations, this appears to be a reasonable strategy to reduce CR-BSI. These benefits should be weighed with heparin's potential side effects, which include heparin-induced thrombocytopenia and bleeding.

Tunneling Short-Term CVCs

Because the primary site of entry for microorganisms on the CVC is the site of cutaneous insertion, tunneling the catheter in the subcutaneous tissue may decrease the incidence of infection. Several trials have evaluated the effect of tunneling on catheter-related infection; a recent meta-analysis has summa-

rized the potential benefit (32). The meta-analysis included seven trials (only two of which focused on critical care patients) and found that compared with patients receiving standard catheter placement, tunneling decreased bacterial colonization (RR, 0.61; 95% CI, 0.39–0.95) and decreased CR-BSI (RR, 0.56; 95% CI, 0.31–1) (32). However, the benefit of tunneling came primarily from one trial using the internal jugular as the site of catheter placement; the reduction in CR-BSI no longer reached statistical significance when data from the several subclavian catheter trials were pooled (RR, 0.71; 95% CI, 0.36–1.43) (32). The authors concluded appropriately that current evidence does not support the routine use of tunneling CVCs until tunneling efficacy is clearly demonstrated at different placement sites and relative to other interventions (e.g., antimicrobial catheters) (32).

Summary of Preventive Methods against CVC-related Infection

Infections due to CVCs are common among the critically ill and lead to substantial morbidity and healthcare costs. Several new methods will likely reduce the incidence of this common patient safety problem, including the use of: (1) maximum sterile barriers during catheter insertion; (2) CVCs coated with an antimicrobial agent; and (3) CHG at the insertion site. Additionally, avoiding both unnecessarily prolonged central venous catheterization and catheterization of the femoral vein are important methods of reducing infection rates. Finally, assiduously adhering to proper hand hygiene and infection control principles still remain crucial practices for preventing CVC-related bloodstream infection.

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