Preventing Arterial Catheter-Associated Bloodstream Infections: Common Sense and Chlorhexidine*

James D. Chalmers, MD
Stefano Aliberti, MD
Tayside Respiratory Research Group
University of Dundee
Dundee, United Kingdom; and
Department of Health Science
University of Milan Bicocca
Clinica Pneumologica, AO San Gerardo
Monza, Italy

Intravascular catheters are a frequent cause of hospital-acquired infections with at least 80,000 cases of catheter-related infection reported in ICUs in the United States annually (1, 2). Estimates suggest that the true rate of infections is closer to 250,000 annually when intravascular devices throughout hospitals are taken into account (1, 2). The attributable mortality has been reported at 11.5% with up to an additional 12 days of ICU stay attributed to catheter-related infections (2, 3). This represents an important source of preventable patient morbidity and mortality.

All vascular access devices carry a risk of infection, with the lowest risk associated with peripheral venous catheters (0.5 cases per 1,000 d) and the highest risk associated with central venous catheters (reported to be 2.7 per 1,000 catheter days in one systematic review, and between 1 and 3.1 per 1,000 d across European studies) (1, 4).

In contrast to central venous catheters where a large effort has been committed to developing bundles of care to reduce infection rates (5, 6), less is known about arterial catheter infections. As arterial catheters are frequently used both in the ICU and in an increasing number of care settings outside the ICU (such as, coronary care units and high dependency units), understanding the prevalence and risk factors for arterial catheter-associated infections is important.

In this issue of *Critical Care Medicine*, O'Horo et al (7) report a systematic review and meta-analysis of published observational studies describing the prevalence of bloodstream infections associated with arterial catheters (7). They studied data from 30,841 arterial catheters inserted in patients with critical illness or following surgery. The definition of catheter-related bloodstream infection was appropriate, including correlating a catheter culture with a positive blood culture and signs and symptoms consistent with sepsis. The primary outcome was to determine the prevalence of arterial catheter-related infection (7).

A major finding of the analysis was if clinicians actively look for arterial catheter infections, they will find more than expected. The rate of diagnosis of arterial catheter-associated infection was 0.7 cases/1,000 catheter days in those studies that only performed cultures when infection was "suspected to be from the catheter" almost doubling to 1.26/1,000 catheter days when cultures were routinely performed from arterial catheters in patients with suspected infection. Although lower than the prevalence reported with central venous catheters, this supports the view that arterial catheters are an underrecognized source of infection and should always be considered a potential source (7).

The key question, of course, is how do we prevent the development of catheter-associated infections? The analysis by O'Horo et al (7) was unable to establish what sterile precautions during insertion are effective in preventing these infections, and no preprocedure cleaning regime was shown to be clearly superior. There was, however, a significant benefit demonstrated of using chlorhexidine-impregnated dressings (risk ratio [RR], 0.35; 95% CI, 0.31–0.91) based on three studies (8–10). This is the only part of the analysis that was based on randomized controlled trial data and would strongly support this practice. Although there has been concern over the prevalence of contact dermatitis associated with use of the chlorhexidine dressings, the frequency of this, at 1.1% in one study (10), appears modest and guidelines recommend use of these dressings where existing methods of reducing catheter-associated infections have not been effective (11).

In keeping with guidelines recommendations, the analysis clearly demonstrates that the femoral site should be avoided whenever possible for arterial catheter placement (7, 11). Femoral catheters were associated with a near doubling of the risk of bloodstream infection (RR, 1.94; 1.32–2.84) in this analysis. Guidelines also suggest that if use of the femoral site is required, then full aseptic precautions as for central venous catheters should be observed (11).

Other sensible measures which could not be addressed in the present study include removing the catheter as soon as it is no longer needed, as there is a direct link between the duration of catheterization and infection risk. In addition to these recommendations, the increasing availability and familiarity with bedside ultrasound makes ultrasound-guided procedures increasingly the norm. Ultrasound-guided vascular access has

*See also p. 1334.

Key Words: arterial; bacteremia; catheter; healthcare-associated infections; infection

Dr. Chalmers holds grants from the Wellcome Trust, MRC, Chief Scientists Office, Tenovus Scotland, and Bayer HealthCare. He received fees for lectures from Glaxosmithkline, Astrazeneca, and Chiesi. His institution consulted for Bayer HealthCare. Dr. Aliberti consulted for Bayer; lectured for Zambon, Boehringer Ingelheim, Pfizer, Novartis, BRAHMS, GlaxoSmithKline, Menarini, Merck Sharp & Dohme, Nycomed, Abbott, and Bayer; and received royalties from McGraw Hill.

DOI: 10.1097/CCM.0000000000000240

been shown to shorten time of the procedure, reduce the number of failed puncture attempts, and minimize complications of catheterization, including infections (11). This can be considered for radial artery catheterization.

The 2011 update of the Centre for Disease control guidelines for the prevention of intravascular catheter-related infections makes several recommendations that are now reinforced by the present data (12). These include the following:

- Use of the radial, brachial, or dorsalis pedis sites and avoidance of the femoral and axillary sites.
- Use of a minimum of cap, mask, sterile gloves, and fenestrated drape for insertion.
- Maximal sterile procedures for axillary or femoral insertion.
- Replace catheters only when clinically indicated and do not routinely replace catheters to prevent infection.
- Removal as soon as the catheter is no longer needed.
- Using disposable transducers and replacing these along with the other components of the system at 96-hour intervals.

Experience from guidelines with central venous catheters shows that guideline compliance is often suboptimal and varies greatly between ICUs. A survey of 25 ICUs in the United States, for example, found only 28% required maximal sterile precautions for central venous catheter insertion. Sixteen percent of units routinely replaced catheters to reduce infection rates, against the guideline recommendation to avoid this (13). There are limited data regarding arterial catheter guideline compliance specifically, but what published data exists suggests practice is also suboptimal (14).

The message of this work is clear—arterial catheters are a source of infection like all other vascular devices, and sensible precautions and practices can reduce the prevalence of hospital-acquired infections. When managing arterial catheters, use some common sense and some chlorhexidine.

REFERENCES

1. Maki DG, Kluger DM, Crnich CJ: The risk of bloodstream infection in adults with different intravascular devices: A systematic review of 200 published prospective studies. *Mayo Clin Proc* 2006; 81:1159–1171
2. Soufir L, Timsit JF, Mahe C, et al: Attributable morbidity and mortality of catheter-related septicemia in critically ill patients: A matched, risk-adjusted, cohort study. *Infect Control Hosp Epidemiol* 1999; 20:396–401
3. Renaud B, Brun-Buisson C; ICU-Bacteremia Study Group: Outcomes of primary and catheter-related bacteremia. A cohort and case-control study in critically ill patients. *Am J Respir Crit Care Med* 2001; 163:1584–1590
4. Suetens C, Morales I, Savey A, et al: European surveillance of ICU-acquired infections (HELICS-ICU): Methods and main results. *J Hosp Infect* 2007; 65(Suppl 2):171–173
5. Pronovost PJ, Goeschel CA, Colantuoni E, et al: Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: Observational study. *BMJ* 2010; 340:c309
6. Marsteller JA, Sexton JB, Hsu YJ, et al: A multicenter, phased, cluster-randomized controlled trial to reduce central line-associated bloodstream infections in intensive care units. *Crit Care Med* 2012; 40:2933–2939
7. O'Horo JC, Maki DG, Krupp AE, et al: Arterial Catheters as a Source of Bloodstream Infection: A Systematic Review and Meta-Analysis. *Crit Care Med* 2014; 42:1334–1339
8. Lucet JC, Bouadma L, Zahar JR, et al: Infectious risk associated with arterial catheters compared with central venous catheters. *Crit Care Med* 2010; 38:1030–1035
9. Timsit JF, Schwebel C, Bouadma L, et al; Dressing Study Group: Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: A randomized controlled trial. *JAMA* 2009; 301:1231–1241
10. Timsit JF, Mimoz O, Mourvillier B, et al: Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med* 2012; 186:1272–1278
11. Maecken T, Grau T: Ultrasound imaging in vascular access. *Crit Care Med* 2007; 35:S178–S185
12. O'Grady NP, Alexander M, Burns LA, et al; Healthcare Infection Control Practices Advisory Committee: Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control* 2011; 39:S1–34
13. Warren DK, Yokoe DS, Climo MW, et al: Preventing catheter-associated bloodstream infections: A survey of policies for insertion and care of central venous catheters from hospitals in the prevention epicenter program. *Infect Control Hosp Epidemiol* 2006; 27:8–13
14. Reynolds H, Dulhunty J, Tower M, et al: A snapshot of guideline compliance reveals room for improvement: A survey of peripheral arterial catheter practices in Australian operating theatres. *J Adv Nurs* 2013; 69:1584–1594

Arterial Catheters as a Source of Bloodstream Infection: A Systematic Review and Meta-Analysis*

John C. O'Horo, MD[1]; Dennis G. Maki, MD, MS[2]; Anna E. Krupp, RN[3]; Nasia Safdar, MD, PhD[2,3,4]

Objective: Catheter-related bloodstream infections are associated with significant costs and adverse consequences. Arterial catheters are commonly used in the critical care setting and are among the most heavily manipulated vascular access devices. We sought to evaluate the prevalence of arterial catheter-related bloodstream infection.

Data Sources: PubMed, CinAHL, EMBASE, and Web of Science.

Study Selection: Included studies reported prevalence rate of catheter-related bloodstream infection for arterial catheters used for critical illness or postoperative monitoring. For the purposes of this study, catheter-related bloodstream infection was defined as positive blood culture collected from an arterial catheter and from the periphery with the same organism in a patient demonstrating systemic signs of sepsis.

Data Extraction: The study population, site of insertion, antiseptic preparation, catheter days, and prevalence of catheter-related bloodstream infection were abstracted. When data were not available, authors were contacted for further information.

Data Synthesis: Forty-nine studies met criteria including 222 cases of arterial catheter-related bloodstream infection in 30,841 catheters. Pooled incidence was 3.40/1,000 catheters or 0.96/1,000 catheter days. Prevalence was considerably higher in the subgroup of studies that cultured all catheters (1.26/1,000 catheter days) compared with those studies that cultured only when the arterial catheter was suspected as the source for the catheter-related bloodstream infection (0.70/1,000 catheter days). Pooled data also found a significantly increased risk of infection for femoral site of insertion compared with radial artery for arterial catheter placement (relative risk, 1.93; 95% CI, 1.32–2.84; $p = 0.001$)

Conclusions: Arterial catheters are an underrecognized cause of catheter-related bloodstream infection. Pooled incidence when catheters were systematically cultured and correlated to blood culture results indicated a substantial burden of arterial catheter-related bloodstream infection. Selection of a radial site over a femoral site will help reduce the risk of arterial catheter-related bloodstream infection. Future studies should evaluate technologies applied to preventing central venous catheter-related bloodstream infection to arterial catheters as well. (*Crit Care Med* 2014; 42:1334–1339)

Key Words: arterial catheterization; catheter-related infections; critical care; meta-analysis; nosocomial infections; peripheral; prevalence

Arterial catheters are essential for hemodynamic monitoring in critically ill patients. Each year, approximately eight million arterial catheters are placed in the United States (1, 2). One of the most serious complications of all intravascular devices is catheter-related bloodstream infection (BSI) (3). Arterial catheter-related BSIs (CRBSIs) are associated with serious complications, including site pseudoaneurysms (4), septic thromboarteritis (5), and arterial rupture (6). Arterial CRBSIs carry a considerable risk of morbidity and mortality, as complications often require surgical intervention. The risk of endemic arterial CRBSI is unclear and has ranged from 0% to 4% in published studies (7, 8). A meta-analysis conducted in 2000 which included six prospective studies in adults determined the incidence of arterial CRBSI to be 2.9 per 1,000 catheter days, a rate close to that seen with short-term noncuffed central venous catheters (CVCs, 2.5 per 1,000 CVC days) (9). In the intervening decade, several more studies have been published about the arterial catheter as a source of BSI, but it remains an underrecognized source of BSI. We undertook a systematic review and meta-analysis to determine the prevalence of BSI associated with arterial catheters.

***See also p. 1533.**

[1]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN.

[2]William S. Middleton Memorial Veterans Hospital, Madison, WI.

[3]Section of Infectious Diseases, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI.

[4]University of Wisconsin Hospital and Clinics, Madison, WI.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccmjournal).

The authors have disclosed that they do not have any potential conflicts of interest.

Address requests for reprints to: Nasia Safdar, MD, PhD, UW Medical Foundation Centennial Building, 1685 Highland Avenue, Madison, WI 53705-2281. E-mail: ns2@medicine.wisc.edu

DOI: 10.1097/CCM.0000000000000166

METHODS

Search Strategy and Data Abstraction

With the aid of an expert librarian, MEDLINE, CinAHL, EMBASE, and the Cochrane review database were searched from inception to December 2012 for articles on BSI in arterial catheters without publication date restrictions. Search terms were "Catheter-related infections/ep,mo,pc AND (BSI OR bloodstream OR "blood stream" OR bacteremia* or bacteraemi*)," (Catheter-related infections/ OR "catheter related" OR "catheter-associated" or PICC or "peripherally inserted") AND (BSI OR bloodstream OR "blood stream" OR bacteremia* or bacteraemia* or blood/mi or septic*) AND (epidemiology*(tw,fs) or incidence)" and "Catheter related bacteremia/ep OR (catheter infection/ep and blood stream infection)."

Inclusion criteria for review were human trials or reports that evaluated BSI in arterial catheters. Studies using arterial catheters for reasons other than critical illness and postsurgical monitoring (e.g., part of an extracorporeal membrane oxygenation or bypass circuit, arterial chemotherapy delivery) were excluded. No language restrictions were applied. References of all relevant articles, including reviews and editorials, were manually inspected for potentially relevant studies. The search strategy was in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement (10).

Included studies had to have a definition of arterial CRBSI including correlation of a catheter tip culture to a separate blood culture with signs and symptoms compatible with sepsis and no other source identified. Data abstracted from each study included the study design, whether or not all catheters were cultured, practitioner who inserted the arterial catheter, site of insertion, whether full barrier precautions were used, agents for cutaneous antisepsis, any other adjunctive methods used for infection prevention such as a chlorhexidine sponge, total number of catheters with BSI, catheter colonization, total number of catheters, and number of catheter days. If multiple articles reported data from the same population, these were combined into a single dataset for analysis. When necessary, authors were contacted for additional information.

Study Outcomes

The purpose of this meta-analysis was to determine the prevalence of arterial CRBSI. This was determined by pooling the observed rates of catheter infection in studies where all catheters were cultured and comparing with studies where arterial catheters were cultured only when they were suspected as a source of BSI.

Secondary endpoints included catheter infection rates observed at different sites (e.g., radial vs femoral) and insertion techniques, such as barrier precautions, site preparations, and maintenance techniques, such as chlorhexidine-impregnated sponge dressings.

Data Analysis

Incidence rates of infection for each study were calculated for infections per 1,000 arterial catheters and infections per 1,000 catheter days. CIs of infections per 1,000 catheter days were calculated using a Freeman-Tukey transformation to adjust Poisson-distributed data to the normal curve (11). Estimated variances were calculated by adding a proportionality constant to the observed number of infections to adjust for values of zero as the reciprocal of the number of subjects in that study.

To evaluate if prevalence of arterial CRBSI is underestimated, infection rates were pooled in studies where all catheter were cultured versus in studies where catheters were cultured only if the arterial catheter was suspected as the source of CRBSI. Resultant data were pooled using the random effects model prescribed by Dersimonian and Laird (12). Because of the limitations inherent to pooling rates in noncomparative studies, subgroup analyses for the impact of site selection and use of infection control measures like chlorhexidine-impregnated sponge were restricted to comparative studies evaluating these endpoints. Risk ratios were combined using the fixed-effects modeling. Heterogeneity was assessed with an I^2 statistic where 0% indicates no heterogeneity and 100% indicates the highest level of heterogeneity. Data were analyzed using Stata 12 software (StataCorp, College Station, TX) (13) with the aid of the Metan package (14).

RESULTS

Search Summary

A total of 970 articles were found using the search strategy described. An additional 187 articles were found through manual inspection of references and other sources. Following removal of duplicates, a total of 1,153 distinct articles remained. Of these, 1,062 were excluded based on abstract information, and 42 were excluded based on full-text review, leaving 49 studies which met criteria for inclusion. This is summarized as a PRISMA diagram in **Figure 1**.

Several publications drew from common datasets; both Koh et al (15) and Koh et al (16) reported different findings from the same study data, as did Lucet et al (17) and Timsit et al (18). Both the studies by Lorente et al (19, 20) and Lorente et al (21) included reporting from the same set of data, leaving 46 distinct datasets for this analysis.

Study Characteristics

Studies were conducted from 1970 to 2012. All studies reported the total number of arterial catheters for a total of 35,465. Catheter days were reported in 34 studies reporting 182,768 catheter days (7, 8, 15, 16, 18–47). Three studies were in neonates (22, 23, 32), one study was in children (47), one included both children and adults (15), and the remaining 44 included only adults (7, 8, 16–21, 24–31, 33–46, 48–61).

Forty-two studies were restricted to ICUs and patients receiving critical illness monitoring (7, 8, 15–23, 25–28, 30–38, 40–45, 47, 50–60) and seven included postsurgical patients requiring close monitoring (8, 22, 23, 24–26, 28, 29, 33, 37–43, 46, 48, 49, 51, 52, 56, 59, 61) (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/A871).

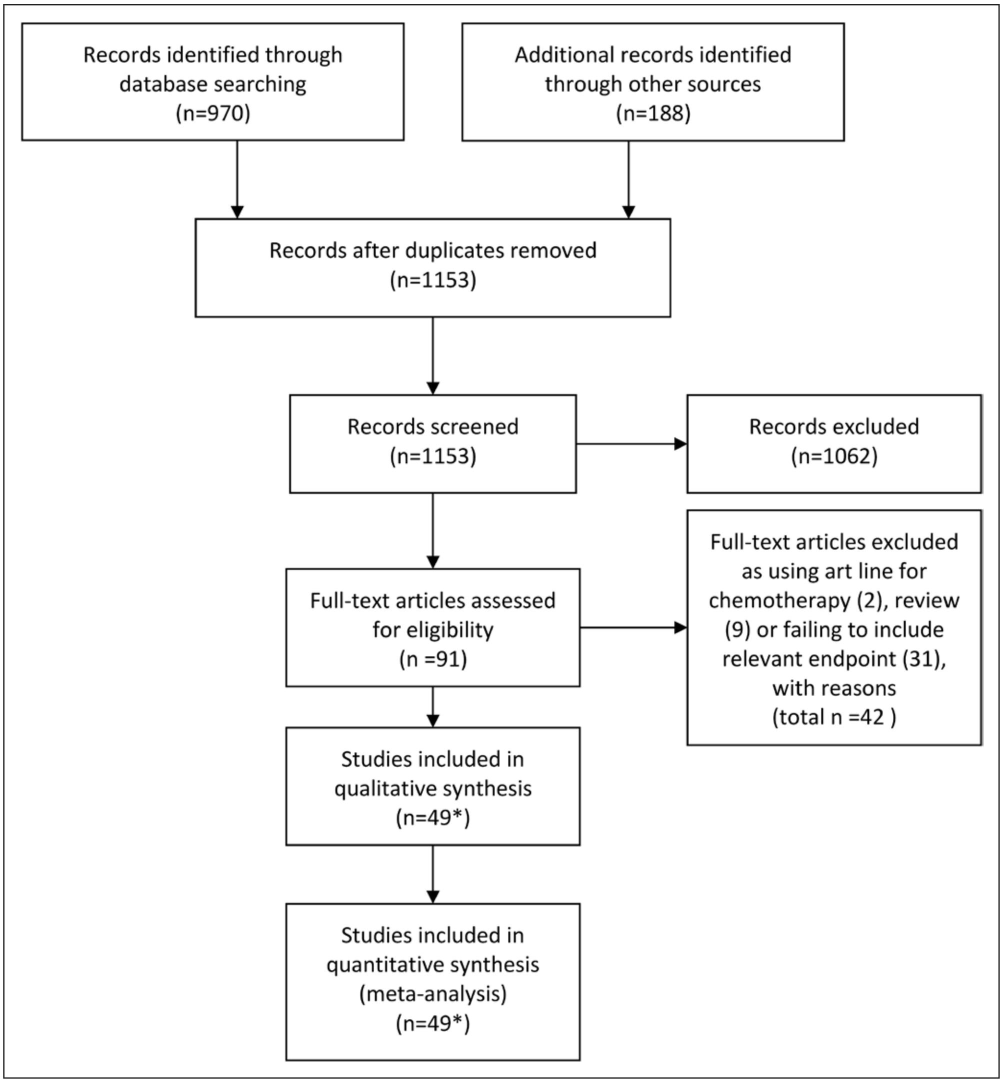

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analysis flow diagram. Flowsheet illustrates search strategy and identification of relevant articles. *49 publications including 46 distinct datasets.

CRBSI

Two hundred two cases of arterial CRBSI were reported in 30,841 arterial catheters. Pooled incidence of CRBSI using a random effects model was 3.40/1,000 catheters (95% CI, 3.39–3.41/1,000 catheters). The rate was 0.96/1,000 catheter days in studies reporting that denominator (95% CI, 0.84–1.12 CRBSI/1,000 catheter days). However, although 26 studies cultured all catheters (7, 15–21, 24, 27, 30–32, 34–36, 44, 45, 47, 48, 50, 53–55, 57, 58, 60), 17 only cultured the catheter if it was suspected as the source of infection. When examined as catheter days, the rate in studies with all catheters cultured was 1.26/1,000 catheter days (1.05–1.52/1,000 catheter days) compared with 0.70/1,000 (95% CI, 0.55–0.87/1,000 catheter days) in other studies.

In subgroup analyses of age, the prevalence of arterial CRBSI in studies of adults was not significantly different from the overall population; this is likely because they comprised the majority of cases, with 254 infections reported in 35,465 catheters, making up 97.2% of the pooled study population. Children could not be analyzed as a separate subgroup because only one study specifically investigated this population. Three studies in the neonatal population reported 10 arterial CRBSI across 356 catheters and 9,586 catheter days (22, 23, 32). When restricted to the neonatal population, overall infection rate was considerably higher at 18/1,000 catheters or 2/1,000 catheter days. Of note, all of the infections seen in neonates occurred in one study of umbilical arterial catheters which was the only one to culture all catheters (32).

Site

Of the studies reporting outcomes by site, 26 studies reported outcomes for the radial artery (7, 8, 17, 18, 22–24, 27, 31, 33–35, 39, 42–49, 53, 57, 59–61), 19 for the femoral artery (7, 8, 17, 19, 20, 24, 25, 27, 29, 31, 34, 35, 42–45, 47, 48, 53), 10 for the brachial artery (7, 19, 20, 24, 34, 35, 44, 47–49), 10 for dorsalis pedis artery (7, 19, 20, 24, 34, 35, 39, 47–49), and two for the ulnar artery (24, 48) as the site of insertion.

Femoral site CRBSI occurred in 1.5% of all catheters (95% CI, 0.8–2.2%), which is higher than radial CRBSI (0.3%, 95% CI, 0.1–0.4%). In the subset of true comparative studies which included both a femoral and a radial arm (8, 17, 18, 24, 27, 31, 34, 35, 42, 47, 48, 53), arterial catheters placed at the femoral site had a relative risk of infection 1.94 times greater than those placed at the radial site (95% CI, 1.32–2.84; $p = 0.001$; $I^2 = 17\%$) (**Fig. 2**).

Sterile Practices

One study reported conducting insertion as a nonsterile procedure (28), 10 reported using sterile gloves only (7, 15, 16, 25, 29, 30, 36, 42, 53, 54), and 23 inserted arterial catheters using gown, cap, mask, and full barrier drape (17–21, 24, 26, 27, 31, 32, 34, 35, 37, 38, 40, 44–46, 49, 50, 56, 58, 60). One study specifically evaluated the impact of full barrier precautions versus using sterile gloves only and did not find any significant difference in BSI. It is, however, worth noting that this study only included peripheral arterial catheters (dorsalis pedis and radial catheters), and to our knowledge, no study has evaluated the impact of maximal barrier precautions for femoral, axillary, and brachial arterial catheters.

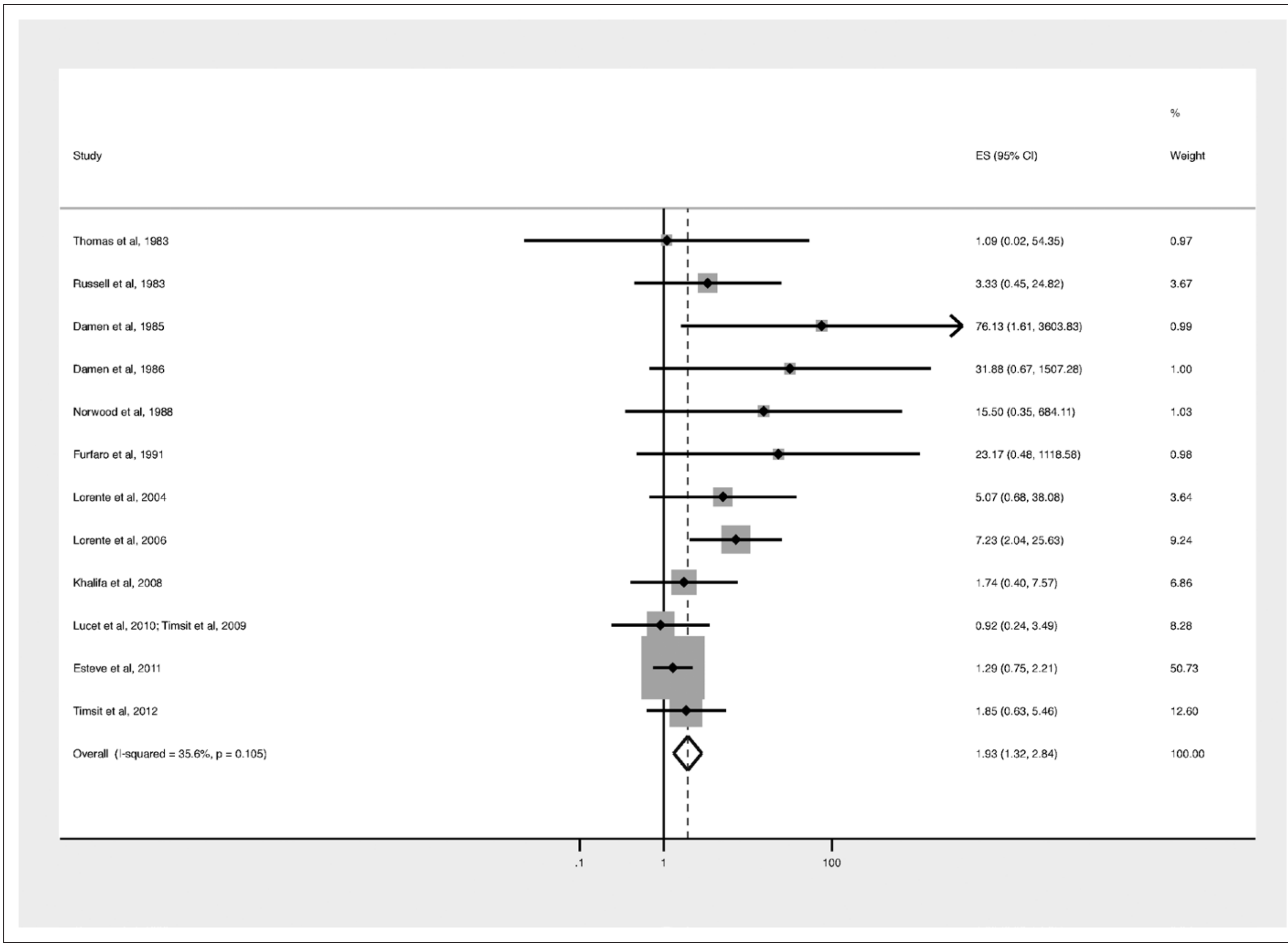

Figure 2. Forest plot of radial versus femoral catheter with regard to risk of infection. *Solid lines* denote CIs of effect size (ES) estimate for individual studies, *box sizes* denote the study weighting, *dashed line* denotes the combined ES, and the *diamond* denotes the CI for the overall effect size.

Site Cleaning

Cutaneous antisepsis regimens fell into three categories: povidone-iodine-based, isopropyl alcohol–based, and chlorhexidine gluconate–based solutions. One small study ($n = 64$) compared using povidone-iodine with a triclosan solution, used in conjunction with regular site cleaning and a transparent dressing. No infections were seen in either group (59). Another study was a randomized controlled trial, comparing 2% chlorhexidine, povidone-iodine, and isopropyl alcohol for both arterial catheters and CVCs. Although the study found superiority of chlorhexidine overall, the arterial catheter subgroup analysis did not find a statistically significant advantage for chlorhexidine over povidone-iodine (RR, 1.01; 95% CI, 0.99–1.03) nor 70% isopropanol (RR, 1.00; 95% CI, 0.99–1.02) (36).

Maintenance Practices

Chlorhexidine-impregnated dressings were used in four studies (17, 18, 27, 45) comprising three distinct datasets. One of these was a noncomparative study, reporting an infection rate of 3.53/1,000 catheter days overall despite consistent use of a sterile gauze dressing impregnated with chlorhexidine pomade (27). The other two were comparative, comparing the use of a commercially available chlorhexidine sponge product (Bio-Patch; Ethicon, Somerville, NJ) or dressing (Tegaderm CHG Chlorhexidine IV securement Dressing; 3M, St. Paul, MN) with no sponge for both arterial and venous catheters. Pooled data from both studies found that the risk of infection was significantly decreased with use of chlorhexidine-impregnated dressings in the arterial catheter subgroup (RR = 0.35, 95% CI, 0.13–0.91, $I^2 = 0\%$) (17, 18, 45).

DISCUSSION

Our study has several major findings. First, our analyses show that the arterial catheter represents an underappreciated source of BSI; there was an increased infection rate seen in studies which cultured all catheters and correlated with blood cultures, compared with those which cultured arterial catheters only when clinical suspicion of the arterial catheter as a source for CRBSI was high. The rate seen in the systematically cultured arterial catheters of 1.6 infections/1,000 catheter days is similar to what has been reported for infections associated with short-term CVCs (9).

In our experience, most U.S. intensivists do not consider arterial catheters a significant contributor to BSI. This belief is reflected in the Joint Commission on Accreditation of Healthcare Organizations recommendations for surveillance for CVC associated BSI but not arterial CRBSI. However, arterial catheters are among the most heavily manipulated devices in the critical care or operating room environment and clearly represent a potential threat of BSI.

Second, we found that the site and manner of arterial catheter implantation has relevance when it comes to prevention of BSI. Preferentially avoiding the femoral site, when feasible, is advisable. Use of maximal sterile precautions for radial and dorsalis pedis catheter insertions did not reduce infections in the one comparative study, but this finding should not be extended to central arterial catheter insertions as noted in current guidelines (62). Use of chlorhexidine sponge and chlorhexidine skin preparations is associated with significant reductions in arterial CRBSI and is also endorsed by current guidelines (62).

Our study has limitations stemming from the designs of the included studies. First, the practice of drawing blood cultures from arterial catheters makes differentiating colonization from CRBSI difficult and limited the number of studies which we could include. Second, although it would be of interest to examine duration of catheter placement as a risk for BSI, few studies have prospectively evaluated risk factors for arterial catheters (7, 56). Two studies identified duration of catheter placement more than 4 days, local inflammation, and insertion by cut down to be significant risk factors (7, 56), and one study comparing rates of CRBSI before and after a policy of routinely changing catheters after 5 days found a significant reduction in CRBSI rates (3.13/1,000 catheter days before vs 1.01/1,000 catheter days after, $p < 0.001$). However, overall, there is a paucity of data addressing this question, and the most recent Hospital Infection Control Practices Advisory Committee prevention guideline does not recommend routine replacement of arterial catheters after a specified interval (62). We were not able to address the relative safety of brachial, axillary, dorsalis pedis, or cubital arterial catheter sites due to the small number of studies investigating their safety. Likewise, we could not assess the impact of different practitioners performing insertion (residents, anesthesiologists, and respiratory therapists) on arterial catheter infections. Finally, there is a lack of research on maintenance practices; a small number of studies looked at dressing change intervals, but variability was too high to make a recommendation on the optimal interval of dressing change. No study evaluated the frequency of arterial catheter manipulation, another potentially relevant factor in maintenance that should be addressed in future studies.

Finally, publication bias is always a concern in systematic reviews and meta-analyses. We undertook a comprehensive search to identify gray literature and contacted experts for additional studies as applicable. It is challenging to meaningfully determine if publication bias exists for prevalence data, but it is likely that there is at least some degree of publication bias in our study.

Our findings have implications for infectious disease and critical care practitioners. When evaluating a patient with cryptogenic bacteremia, the arterial catheter should not be overlooked as a potential source. Also, when deciding if continuing use of the arterial catheter is necessary, intensivists should weigh the risk of infection against the benefit of the device similar to the way they would approach CVCs.

In conclusion, arterial catheters are a significant source for CRBSI with infection rates similar to what is seen in short-term CVCs. Consideration should be given to application of novel technologies, such as chlorhexidine-impregnated sponge, especially in the high-risk group of patients with femoral arterial catheters. In patients with cryptogenic BSI, arterial catheters should be examined as a potential source.

ACKNOWLEDGMENTS

We thank librarian Patricia Erwin for her assistance with the search strategy and Drs. Ousmane Traore, Fadia Haddad, Jean-Christophe Lucet, Francesco Esteve-Urbano, John Gowardman, Romain Pirrachio, and Jean-Francois Timsit for responding to requests for unpublished information.

REFERENCES

1. Scheer B, Perel A, Pfeiffer UJ: Clinical review: Complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. *Crit Care* 2002; 6:199–204
2. Maki DG: Pathogenesis, prevention and management of infections due to intravascular devices used for infusion therapy. *In*: Infections Associated with Indwelling Medical Devices. Bisno A, Waldwogel F (Eds). Washington, DC, American Society for Microbiology, 1989, pp 161–77
3. Maki DG: Nosocomial bacteremia. *Am J Med* 1981; 70:183–196
4. Cohen A, Reyes R, Kirk M, et al: Osler's nodes, pseudoaneurysm formation, and sepsis complicating percutaneous radial artery cannulation. *Crit Care Med* 1984; 12:1078–1079
5. Collignon PJ, Munro R, Sorrell TC: Systemic sepsis and intravenous devices. A prospective survey. *Med J Aust* 1984; 141:345–348
6. Arnow PM, Costas CO: Delayed rupture of the radial artery caused by catheter-related sepsis. *Rev Infect Dis* 1988; 10:1035–1037
7. Band JD, Maki DG: Infections caused by arterial catheters used for hemodynamic monitoring. *Am J Med* 1979; 67:735–741
8. Thomas F, Burke JP, Parker J, et al: The risk of infection related to radial vs femoral sites for arterial catheterization. *Crit Care Med* 1983; 11:807–812
9. Kluger D, Maki D: The relative risk of intravascular device-related bloodstream infections with different types of intravascular devices in adults. A meta-analysis of 206 published studies. *In*: ICHE, Programs and Proceedings of the Fourth Decennial International Conference on Nosocomial and Healthcare-Associated Infections, Atlanta, GA, 2000, p 95
10. Moher D, Altman DG, Liberati A, et al: PRISMA statement. *Epidemiology* 2011; 22:128
11. Freeman MF, Tukey JW: Transformations related to the angular and the square root. *Ann Math Statist* 1950; 21:607–611
12. DerSimonian R, Laird N: Meta-analysis in clinical trials. *Control Clin Trials* 1986; 7:177–188
13. StataCorp: Stata Statistical Software, Release 12. College Station, TX, StataCorp LP, 2011
14. Ross H, Mike B, Jon D, et al: METAN: Stata Module for Fixed and Random Effects Meta-Analysis. S456798. Boston College Department of Economics, Boston, MA, 2006
15. Koh DB, Gowardman JR, Rickard CM, et al: Prospective study of peripheral arterial catheter infection and comparison with concurrently sited central venous catheters. *Crit Care Med* 2008; 36:397–402

16. Koh DB, Robertson IK, Watts M, et al: A retrospective study to determine whether accessing frequency affects the incidence of microbial colonisation in peripheral arterial catheters. *Anaesth Intensive Care* 2010; 38:678–684
17. Lucet JC, Bouadma L, Zahar JR, et al: Infectious risk associated with arterial catheters compared with central venous catheters. *Crit Care Med* 2010; 38:1030–1035
18. Timsit JF, Schwebel C, Bouadma L, et al; Dressing Study Group: Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: A randomized controlled trial. *JAMA* 2009; 301:1231–1241
19. Lorente L, Jiménez A, Jiménez JJ, et al: Higher arterial catheter-related infection rates in femoral than in dorsalis pedis access. *J Hosp Infect* 2010; 74:365–369
20. Lorente L, Jiménez A, Martín MM, et al: Lower arterial catheter-related infection in brachial than in femoral access. *Am J Infect Control* 2010; 38:e40–e42
21. Lorente L, Jiménez A, Martín MM, et al: Lower incidence of catheter-related bloodstream infection in cubital than in femoral artery access. *Scand J Infect Dis* 2011; 43:814–817
22. Adams JM, Rudolph AJ: The use of indwelling radial artery catheters in neonates. *Pediatrics* 1975; 55:261–265
23. Adams JM, Speer ME, Rudolph AJ: Bacterial colonization of radial artery catheters. *Pediatrics* 1980; 65:94–97
24. Damen J: The microbiological risk of invasive hemodynamic monitoring in adults undergoing cardiac valve replacement. *J Clin Monit* 1986; 2:87–94
25. Ersoz CJ, Hedden M, Lain L: Prolonged femoral arterial catheterization for intensive care. *Anesth Analg* 1970; 49:160–164
26. Esteve F, Pujol M, Limón E, et al: Bloodstream infection related to catheter connections: A prospective trial of two connection systems. *J Hosp Infect* 2007; 67:30–34
27. Esteve F, Pujol M, Pérez XL, et al: Bacteremia related with arterial catheter in critically ill patients. *J Infect* 2011; 63:139–143
28. Gardner RM, Schwartz R, Wong HC, et al: Percutaneous indwelling radial-artery catheters for monitoring cardiovascular function. Prospective study of the risk of thrombosis and infection. *N Engl J Med* 1974; 290:1227–1231
29. Haddad F, Zeeni C, El Rassi I, et al: Can femoral artery pressure monitoring be used routinely in cardiac surgery? *J Cardiothorac Vasc Anesth* 2008; 22:418–422
30. Hammarskjöld F, Berg S, Hanberger H, et al: Low incidence of arterial catheter infections in a Swedish intensive care unit: Risk factors for colonisation and infection. *J Hosp Infect* 2010; 76:130–134
31. Khalifa R, Dahyot-Fizelier C, Laksiri L, et al: Indwelling time and risk of colonization of peripheral arterial catheters in critically ill patients. *Intensive Care Med* 2008; 34:1820–1826
32. Landers S, Moise AA, Fraley JK, et al: Factors associated with umbilical catheter-related sepsis in neonates. *Am J Dis Child* 1991; 145:675–680
33. Leroy O, Billiau V, Beuscart C, et al: Nosocomial infections associated with long-term radial artery cannulation. *Intensive Care Med* 1989; 15:241–246
34. Lorente L, Santacreu R, Martín MM, et al: Arterial catheter-related infection of 2,949 catheters. *Crit Care* 2006; 10:R83
35. Lorente L, Villegas J, Martín MM, et al: Catheter-related infection in critically ill patients. *Intensive Care Med* 2004; 30:1681–1684
36. Maki DG, Ringer M, Alvarado CJ: Prospective randomised trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet* 1991; 338:339–343
37. Martin C, Saux P, Papazian L, et al: Long-term arterial cannulation in ICU patients using the radial artery or dorsalis pedis artery. *Chest* 2001; 119:901–906
38. Misset B, Timsit JF, Dumay MF, et al: A continuous quality-improvement program reduces nosocomial infection rates in the ICU. *Intensive Care Med* 2004; 30:395–400
39. Naguib M, Hassan M, Farag H, et al: Cannulation of the radial and dorsalis pedis arteries. *Br J Anaesth* 1987; 59:482–488
40. Pirracchio R, Legrand M, Rigon MR, et al: Arterial catheter-related bloodstream infections: Results of an 8-year survey in a surgical intensive care unit. *Crit Care Med* 2011; 39:1372–1376
41. Rijnders BJ, Van Wijngaerden E, Wilmer A, et al: Use of full sterile barrier precautions during insertion of arterial catheters: A randomized trial. *Clin Infect Dis* 2003; 36:743–748
42. Russell JA, Joel M, Hudson RJ, et al: Prospective evaluation of radial and femoral artery catheterization sites in critically ill adults. *Crit Care Med* 1983; 11:936–939
43. Soderstrom CA, Wasserman DH, Dunham CM, et al: Superiority of the femoral artery of monitoring. A prospective study. *Am J Surg* 1982; 144:309–312
44. Traoré O, Liotier J, Souweine B: Prospective study of arterial and central venous catheter colonization and of arterial- and central venous catheter-related bacteremia in intensive care units. *Crit Care Med* 2005; 33:1276–1280
45. Timsit JF, Mimoz O, Mourvillier B, et al: Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med* 2012; 186:1272–1278
46. El-Hamamsy I, Dürrleman N, Stevens LM, et al: Incidence and outcome of radial artery infections following cardiac surgery. *Ann Thorac Surg* 2003; 76:801–804
47. Furfaro S, Gauthier M, Lacroix J, et al: Arterial catheter-related infections in children. A 1-year cohort analysis. *Am J Dis Child* 1991; 145:1037–1043
48. Damen J, Verhoef J, Bolton DT, et al: Microbiologic risk of invasive hemodynamic monitoring in patients undergoing open-heart operations. *Crit Care Med* 1985; 13:548–555
49. Ducharme FM, Gauthier M, Lacroix J, et al: Incidence of infection related to arterial catheterization in children: A prospective study. *Crit Care Med* 1988; 16:272–276
50. Eyer S, Brummitt C, Crossley K, et al: Catheter-related sepsis: Prospective, randomized study of three methods of long-term catheter maintenance. *Crit Care Med* 1990; 18:1073–1079
51. Frezza EE, Mezghebe H: Indications and complications of arterial catheter use in surgical or medical intensive care units: Analysis of 4932 patients. *Am Surg* 1998; 64:127–131
52. Gronbeck C 3rd, Miller EL: Nonphysician placement of arterial catheters. Experience with 500 insertions. *Chest* 1993; 104:1716–1717
53. Norwood SH, Cormier B, McMahon NG, et al: Prospective study of catheter-related infection during prolonged arterial catheterization. *Crit Care Med* 1988; 16:836–839
54. Pinilla JC, Ross DF, Martin T, et al: Study of the incidence of intravascular catheter infection and associated septicemia in critically ill patients. *Crit Care Med* 1983; 11:21–25
55. Puri VK, Carlson RW, Bander JJ, et al: Complications of vascular catheterization in the critically ill. A prospective study. *Crit Care Med* 1980; 8:495–499
56. Raad I, Umphrey J, Khan A, et al: The duration of placement as a predictor of peripheral and pulmonary arterial catheter infections. *J Hosp Infect* 1993; 23:17–26
57. Shinozaki T, Deane RS, Mazuzan JE Jr, et al: Bacterial contamination of arterial lines. A prospective study. *JAMA* 1983; 249:223–225
58. Singh S, Nelson N, Acosta I, et al: Catheter colonization and bacteremia with pulmonary and arterial catheters. *Crit Care Med* 1982; 10:736–739
59. Gabel-Hughes KS, Geelhoed GW: Methods of arterial site skin preparation and dressing. *Crit Care Nurse* 1990; 10:90–96
60. Martin C, Crama P, Courjaret P, et al: [Prolonged catheterization of the radial artery. Prospective evaluation of the thrombogenic and infectious risk]. *Ann Fr Anesth Reanim* 1984; 3:435–439
61. Weiss BM, Gattiker RI: Complications during and following radial artery cannulation: A prospective study. *Intensive Care Med* 1986; 12:424–428
62. O'Grady NP, Alexander M, Burns LA, et al; Healthcare Infection Control Practices Advisory Committee: Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control* 2011; 39:S1–34