

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

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**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

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**\*See also p. 1533.**

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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.

## 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

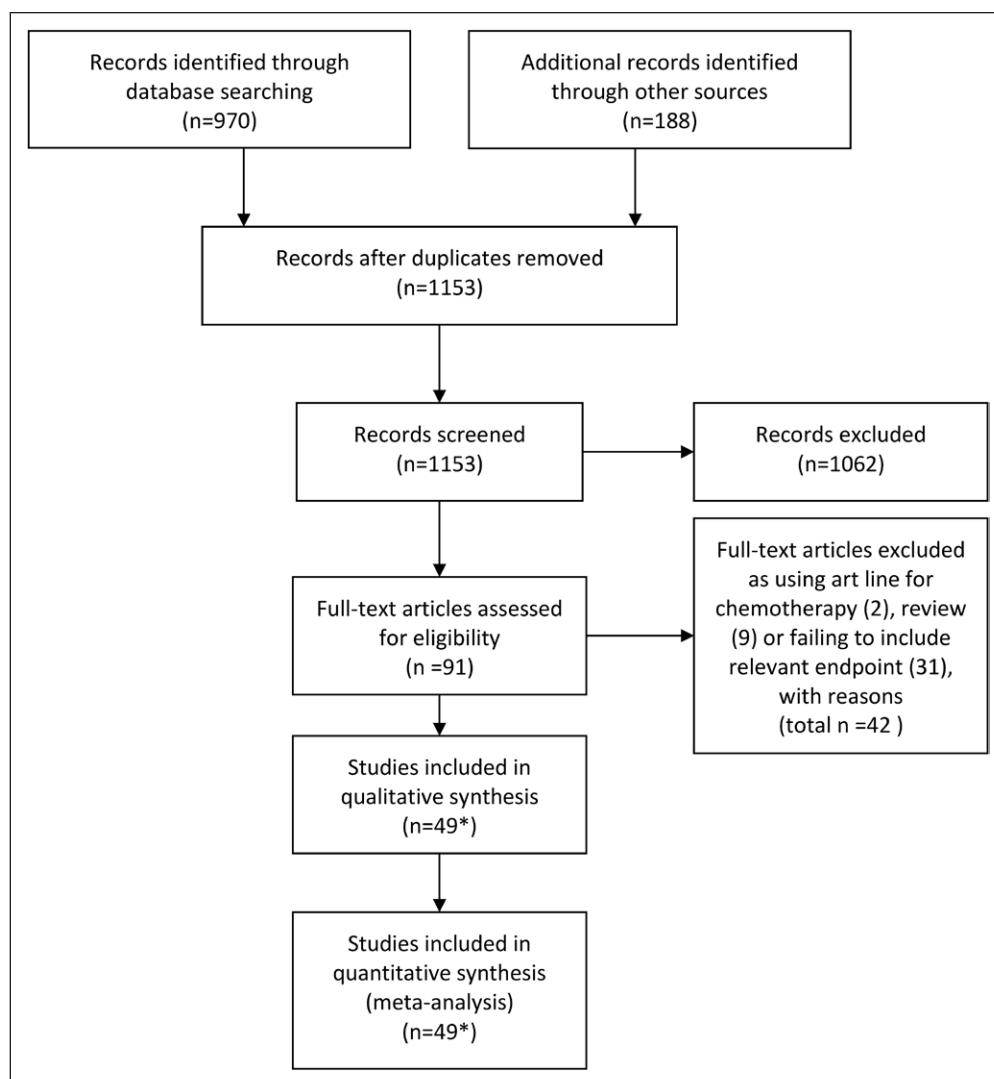
A total of 970 articles were found using the search strategy described. An additional 187 articles were found through manual inspection of references and other sources. Following removal of duplicates, a total of 1,153 distinct articles remained. Of these, 1,062 were excluded based on abstract information, 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

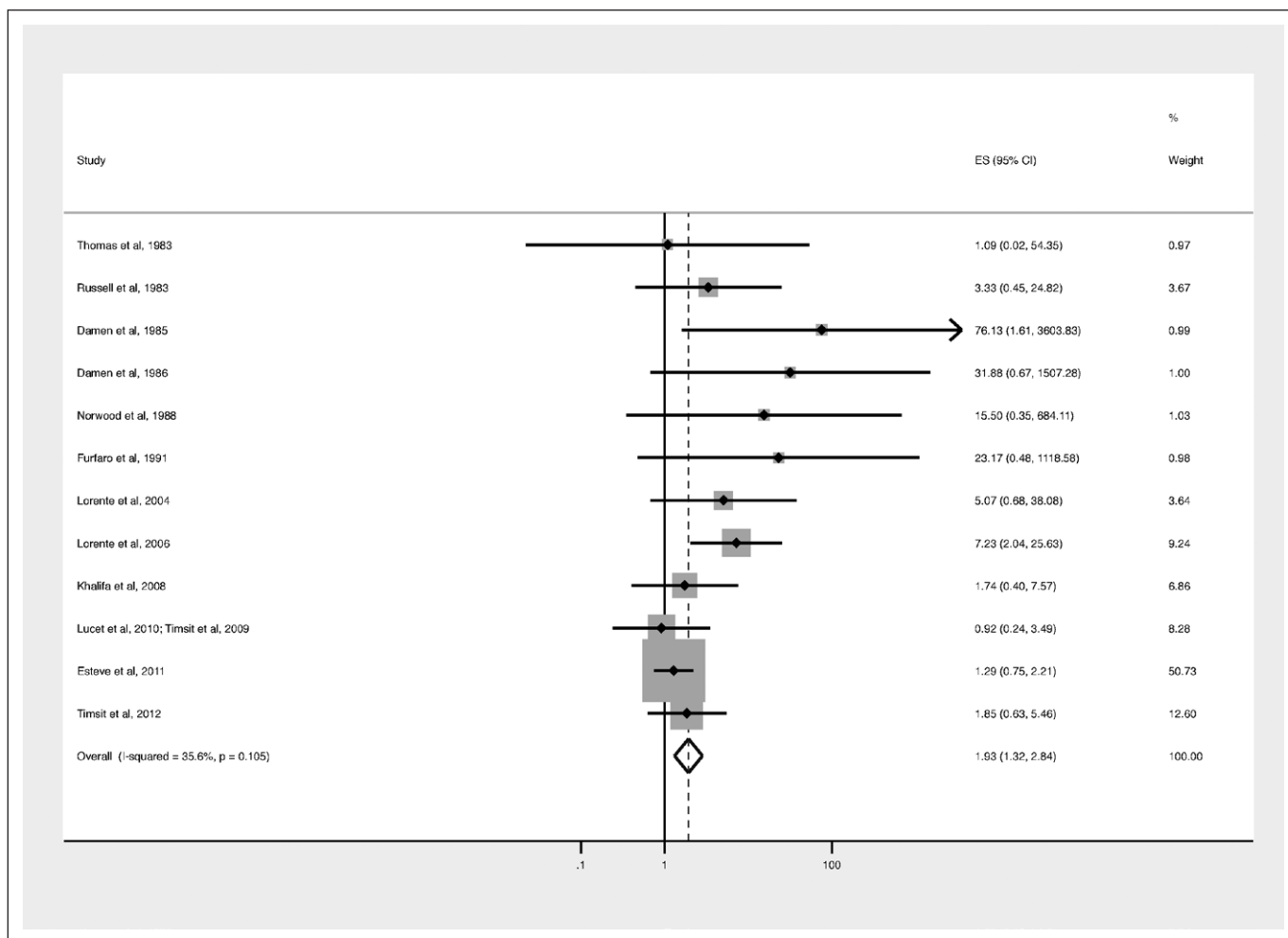
Of the studies reporting outcomes by site, 26 studies reported outcomes for the radial artery (7, 8, 17, 18, 22–24, 27, 31, 33–35, 39, 42–49, 53, 57, 59–61), 19 for the femoral artery (7, 8, 17, 19, 20, 24, 25, 27, 29, 31, 34, 35, 42–45, 47, 48, 53), 10 for the brachial artery (7, 19, 20, 24, 34, 35, 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% isopropyl alcohol (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,  $P = 0\%$ ) (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.

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