

Use of Full Sterile Barrier Precautions during Insertion of Arterial Catheters: A Randomized Trial

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To investigate whether institution of maximal sterile barrier precautions (SBPs) during arterial catheter (AC) insertion prevents catheter colonization, as is the case for central venous catheters (CVCs), a randomized study was conducted. Three hundred seventy-three patients in whom a radial or dorsalis pedis AC was going to be inserted were randomized to an SBP group or a standard-of-care group. These patients, in addition to all patients who were admitted to the unit with an AC already in place or who were not eligible for the randomized study, were observed for AC-related colonization and infection. Data for 272 randomized patients were available for analysis. The colonization incidence was 20.2 cases per 1000 catheter-days in the SBP group and 15.8 cases per 1000 catheter-days in the control group ($P > .1$). AC-related infection occurred in 3 patients in the SBP group and in 7 patients in the control group ($P > .1$). Five episodes of AC-related bloodstream infection were diagnosed (1.5 cases per 1000 catheter-days). Use of SBPs did not prevent AC colonization or infection. The incidence of AC-related infectious complications was comparable to the incidence of CVC-related infection reported in the literature.

Colonization and infection of central venous catheters (CVCs) can be partially prevented using sterile barrier precautions (SBPs) during catheter insertion [1]. These precautions are not normally used during arterial catheter (AC) insertion, yet the majority of patients in the intensive care unit (ICU) are monitored with ACs.

The risk of colonization and infection of ACs might approach that for CVCs, although good data are lacking [2]. The incidence of AC colonization and infection reported in the literature varies considerably, depending on the catheter-tip culture technique used. The highest colonization incidence reported is 27% (49 cases per

1000 catheter-days) [3], and the lowest is 4% (11.7 cases per 1000 catheter-days) [4]. These older studies did not use a standardized catheter culture technique or had small sample sizes. Large studies that use a standardized culture technique are lacking, but 2 smaller studies have reported an estimated rate of colonization of 10%–11% (20–30 cases per 1000 catheter-days) and a rate of catheter-related bloodstream infection (CRBSI) of 1.6%–4.5% (3–13 cases per 1000 catheter-days) [5, 6]. To determine whether use of SBPs during AC placement prevents catheter colonization and infection, and to better estimate the incidences of colonization and infection, we conducted a randomized clinical study.

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PATIENTS, MATERIALS, AND METHODS

Patients. All patients who were hospitalized in the medical ICU of a large university hospital during the period of January 2001 through March 2002 and in whom an AC was going to be placed in the radial or dorsalis pedis site were eligible for the study. No ex-

clusion criteria were used. The catheters used for these insertion sites were made of a fluorinated ethylene propylene polymer (Angiocath; Becton Dickinson Infusion Therapy Systems). After insertion, catheters were dressed with gauze without occlusive dressing, and the gauze was changed only when loosened or soiled. ACs were changed on an as-needed basis, which means that the AC was not changed after a fixed insertion time, but only when clinically necessary (i.e., the AC was not functional anymore, the AC was not needed anymore, or there was suspicion of infection). The arterial lines are used for obtaining blood samples (after disinfection of the hub) several times each day. Femoral and brachial artery catheterization is done by means of the Seldinger technique, which involves the use of a large sterile sheet. Nonsterile manipulation of a guidewire was not acceptable to our ICU physicians for study purposes. Therefore, these insertion sites were not included in the study.

For all catheters, the date of insertion was registered, and, for each patient, we recorded data on underlying disease, age, sex, APACHE II score, and whether sterile gloves had been worn during the entire procedure. During the study period, patients with ACs in place who were not included in the study (i.e., patients who had brachial and femoral catheters inserted in the ICU or who had catheters inserted in the emergency department) were also observed for infection, and their catheters were cultured after removal. The same ACs are used in both the emergency department and the ICU. The study was approved by the institutional review board, which waived the need for informed consent.

Study design. The study was a prospective, randomized trial. Patients were randomly assigned to study groups in a 1:1 ratio by use of dark, nontransparent, sealed, and numbered envelopes that were available in a box in the unit. They were supplied in packs of 16–24 envelopes whenever the previous packs of envelopes were about to be finished. With use of this method, a block randomization with a block size ranging from 16 to 24 patients was achieved. In the SBP group, the AC was placed by health care workers who wore sterile gloves, a mask, a cap, and a sterile gown; a large sterile sheet was used, and procedures were performed after hand washing and disinfection of the patient's skin with 0.5% chlorhexidine in 70% alcohol. In the standard-of-care (SOC) group, the only procedures used were hand washing, wearing of sterile gloves, and skin disinfection with 0.5% chlorhexidine in 70% alcohol.

Culture techniques. After removal (for whatever reason), all ACs were cultured with use of the vortex-sonication technique, and results are reported as the number of colony forming units of organisms per catheter [7]. All intravascular catheters (venous and arterial) were changed in patients who had suspected CRBSI. Strains cultured from the catheters were identified to the species level only when (1) the culture yielded >1000 cfu/catheter, or (2) the AC culture yielded <1000 cfu/

catheter and there was a positive blood culture result. All patients who had their ACs removed because of suspected infection had simultaneous blood samples obtained for culture. These cultures were processed with use of the BacT/Alert Blood Culture System (Organon Teknica).

Diagnosis of catheter-related infection. Removed catheters were classified on the basis of the criteria of Blot et al. [8] with the modifications of Mermel [9]. Catheters were classified as being associated with CRBSI, catheter-related sepsis, or an exit-site infection or as being colonized.

Catheter-related infection was classified as "definite CRBSI" when all of the following criteria were present: symptoms of sepsis disappeared ≤48 h after catheter removal (unless a remote focus of infection that was secondary to CRBSI was responsible for the persistence of sepsis), a positive quantitative catheter-tip culture result (>1000 cfu/catheter) was attained, and the same microorganism was isolated from both the catheter and a peripheral venous blood sample (≥1 positive peripheral-blood culture was required, except for coagulase-negative staphylococci, for which 2 positive blood cultures were required).

Catheter-related infection was classified as "probable CRBSI" when all the criteria for definite CRBSI were fulfilled but only cultures of blood samples obtained through a catheter were available for analysis because it was impossible to obtain peripheral blood samples. Catheter-related infection was also classified as probable CRBSI when all of the criteria for definite CRBSI were fulfilled but the catheter-tip culture yielded a bacterial count of ≤1000 cfu/catheter while patients were receiving antibiotics with activity against the microorganisms recovered from the catheter.

"Catheter-related sepsis" was defined as a positive quantitative catheter-tip culture (>1000 cfu/catheter) for patients with systemic signs of sepsis that disappeared ≤48 h after catheter removal. In these cases, no associated bacteremia was detected or blood culture results were not available. "Exit-site infection" was defined as the presence of erythema, induration, and/or tenderness within 2 cm of the catheter exit site and a positive catheter-tip culture (>1000 cfu/catheter). "Significant colonization of the catheter" was defined as a quantitative catheter-tip culture that yielded >100 cfu/catheter and, when present, symptoms of sepsis that did not resolve ≤48 h after catheter removal.

Statistical analysis. Analysis was performed in accordance with the intention-to-treat principle, according to which patients were analyzed on the basis of the group to which they were randomized, even if SBPs were not followed (e.g., sterile gloves were taken off because of difficulties during insertion). The primary end point was determination of the proportion of positive catheter-tip cultures (>100 cfu/catheter) at the time of removal because of colonization or infection. The secondary

end point was determination of the proportion of AC-related infections.

A 1-sided z test for proportions (Fisher's exact test, when appropriate) was used for comparison of catheter colonization rates between groups. For this purpose and for the power-calculation described below, a 1-sided approach was deemed appropriate because an increase in the rate of infectious complications as a consequence of SBP use is conceptually not understandable. Two-sided tests were used for all other calculations. Student's t test was used for the comparison of means of normally distributed data, and the Mann-Whitney U test was used to compare values that were not normally distributed. Differences were considered to be significant at $P < .05$.

The sample estimate and power calculation were based on (1) available data, from a previous pilot study and from published data on AC colonization in the literature, on the incidence of AC colonization in our medical ICU [5], and (2) the 70% reduction in the rate of catheter colonization observed in the only available study to have investigated the use of SBPs during insertion of CVCs [1, 3–6]. With an estimated rate of colonization of 20 cases per 1000 catheter-days in the SOC group, and with a power of 80% to show a reduction in the rate of colonization of 50% by use of SBPs, 2 groups of 1825 catheter-days each were necessary ($\alpha = 0.05$, by a 1-sided approach). With an average duration of catheterization of 8 days and a dropout rate of 20% resulting from catheter loss, 285 patients were needed for each group. We planned to perform one interim analysis when we reached one-half to two-thirds of the 3650 catheter-days. The interim analysis was performed independently at the Biostatistical Center, School of Public Health, Catholic University (Leuven, Belgium), in accordance with the method of Lan et al. [10], with use of the EaSt-2000 software package, version 1.0 (Cytel Software). For other statistical purposes, SPSS software, version 11.0 (SPSS), and GraphPad Prism, version 3.02 (GraphPad Software), were used.

RESULTS

Baseline features of randomized and analyzable patients are shown in table 1. The characteristics of patients whose AC culture results were not available for the final analysis (mean APACHE II, score 21.5; mean age, 57.9 years) were identical to the baseline characteristics of patients in both the SBP and SOC groups ($P > .1$). The disposition of all patients is shown in figure 1. For 272 of 373 patients who had catheters placed and who were randomized during 14 consecutive months, all data were available for final analysis. A relatively large dropout rate was noted because data for 101 of the randomized patients with catheters (698 catheter-days) were not available for the final analysis. Contamination of the AC during accidental removal (by an agitated patient or during nursing procedu-

Table 1. Baseline characteristics of analyzable patients in a study of the use of sterile barrier precautions during insertion of arterial catheters.

Characteristic	SBP group (n = 129)	SOC group (n = 143)	P
Age, mean years	60.7	60.1	>.1
Female sex, % of patients	43	31	.04
Mean APACHE II score	21.4	20.7	>.1
Duration of catheterization, mean days	8.8	8.4	>.1

NOTE. SBP group, patients who had arterial catheters inserted under sterile barrier precautions; SOC group, patients who had arterial catheters inserted in accordance with the standard of care.

res)—which, therefore, meant that the catheter could not be cultured—was the cause of 51 of these dropouts. Of the 272 analyzable ACs, 44 were removed from patients with a suspected catheter-related infection. Among these 44 patients, 39 intravenous catheters were changed or removed as well, to differentiate between AC- and CVC-related infections. The mean duration of catheterization was 8.8 days in the SBP group and 8.4 days in the SOC group ($P > .1$). Physicians were able to wear gloves during the entire procedures performed for 348 (93.3%) of 373 of patients (SBP group vs. SOC group, $P > .1$).

The study was stopped after the results of the only interim analysis performed were available. The interim analysis showed that the chance of finding a 50% difference in the colonization rate was $<1.5\%$ if the study was continued until 3650 catheter-days were available. Two hundred seventy-two AC-tip cultures (2343 catheter-days) were available for this analysis; 129 of these cultures (1141 catheter-days) were for the SBP group. Twenty-three (17.8%) of the 129 AC-tip culture results (20.2 cases per 1000 catheter-days) were positive in the SBP group, and 19 (13.3%) of 143 AC-tip culture results (15.8 cases per 1000 catheter-days) were positive in the control group, as shown in table 2 ($P > .1$). Because the majority (59 [82%] of 72) of the catheter tips yielded >1000 cfu, the results remained the same regardless of whether a catheter tip cutoff of 100 or 1000 cfu was used.

The incidence of colonization in those patients who were part of the observational study arm (i.e., 133 with ACs inserted in the emergency department and 89 with ACs inserted in the ICU but not included in the study because of femoral or brachial insertion site) was not different from the incidence in the randomized study groups. The incidence among the 133 patients who had ACs inserted in the emergency department (1054 catheter-days) was 17.1 cases per 1000 catheter-days, and the incidence among patients who had ACs inserted in the brachial site in the ICU was 18.6 cases per 1000 days (based on 9 positive tips out of 46 catheters). There were not enough catheters inserted in the femoral site to draw any meaningful conclusions.

Table 3 shows the incidences of different bacteria cultured from all catheters inserted in the ICU during the study and from ACs inserted in the emergency department. Colonization of catheters inserted in the ICU more frequently involved bacteria other than coagulase-negative staphylococci, compared with emergency department catheters.

Six patients had an exit-site infection (1 patient in the SBP group and 5 patients in the SOC group [0.9 cases per 1000 catheter days vs. 4.2 cases per 1000 catheter-days, respectively]; $P = .11$). For these 6 patients, the reason for catheter removal was inflammation of the insertion site, and catheter-tip cultures yielded >1000 cfu/catheter. Four patients had a CRBSI (2 patients in each group [1.8 cases per 1000 catheter-days in the SBP group and 1.7 cases per 1000 catheter-days in the SOC group]; $P > .1$). When data for all patients (from both the randomized study and the observational study) who were admitted to our ICU during the study period are analyzed together, the incidence of definite or probable CRBSI (5 patients) was 1.5 cases per 1000 catheter-days (95% CI, 0.6–3.4 cases per 1000 catheter-days), and the incidence of insertion-site infection was 1.8 cases per 1000 catheter-days (95% CI, 0.8–3.8 cases per 1000 catheter-days). No cases of catheter-related sepsis (as de-

Table 2. Results of primary and secondary end points in a study of the use of sterile barrier precautions during insertion of arterial catheters.

End point	SBP group (n = 129)	SOC group (n = 143)	P
Catheter colonization at time of removal, no. (%) of patients	23 (17.8)	19 (13.3)	>.1
Catheter-related infection, no. of patients (no. of cases per 1000 catheter-days)			
Exit-site infection	1 (0.9)	5 (4.2)	>.1
CRBSI	2 (1.8)	2 (1.7)	>.1
Total	3 (2.6)	7 (5.8)	>.1

NOTE. CRBSI, catheter-related bloodstream infection; SBP group, patients who had arterial catheters inserted under sterile barrier precautions; SOC group, patients who had arterial catheters inserted in accordance with the standard of care.

fined in Patients, Materials, and Methods) were diagnosed. The incidence of catheter-related infection of any kind (i.e., insertion-site infection and CRBSI) was 3.2 cases per 1000 catheter-days (95% CI, 1.8–5.8 cases per 1000 catheter-days).

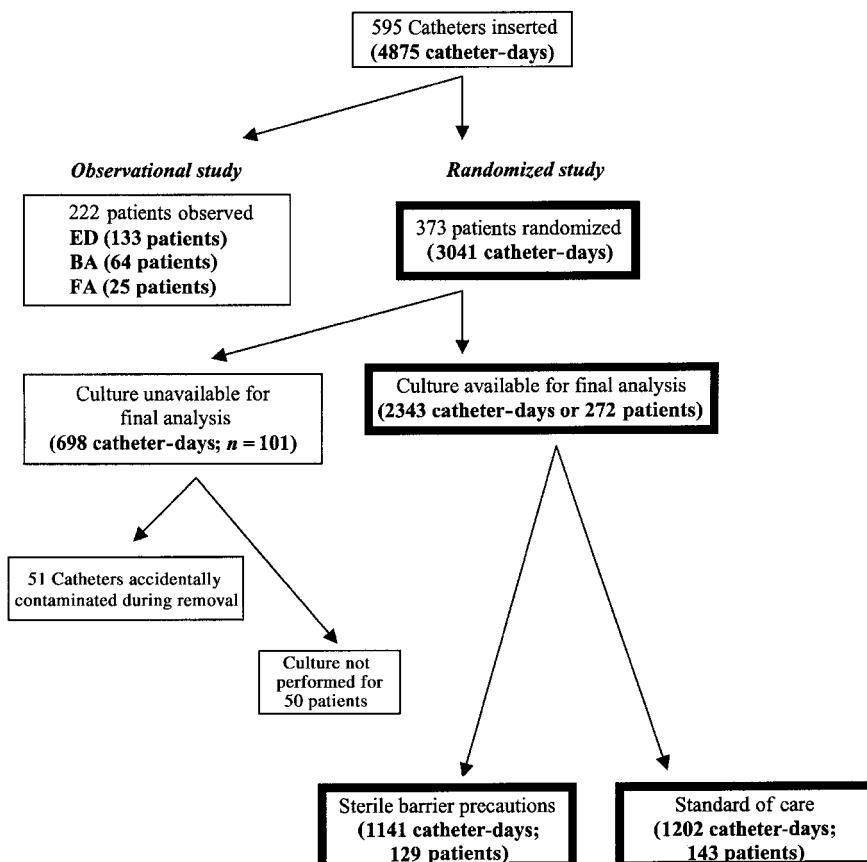


Figure 1. Patient disposition for all randomized and observed patients. BA, arterial catheters inserted in the brachial artery in the intensive care unit (ICU); ED, arterial catheters inserted in the emergency department; FA, arterial catheters inserted in the femoral artery in the ICU.

Table 3. Incidence of specific bacteria grown on catheter-tip cultures in a study of the use of sterile barrier precautions during insertion of arterial catheters.

Bacterium	No. of positive catheter-tip culture results for catheters inserted	
	In the ICU ^a (n = 53)	In the ED (n = 18)
Coagulase-negative staphylococci	32	15 ^b
<i>Staphylococcus aureus</i>	14	0
<i>Pseudomonas</i> species	3	0
Unknown ^c	5	3

NOTE. ED, emergency department; ICU, intensive care unit.

^a Catheters from patients in both the randomized study group and the observational study arm.

^b P = .016, for the difference in the incidence of recovery of non-coagulase-negative staphylococci.

^c Identification was not done for catheter-tip cultures that yielded 100–1000 cfu/catheter if no associated bacteraemia was present.

DISCUSSION

In this randomized study, we found no differences in the incidence of AC colonization when the AC was inserted under full SBPs compared with insertion under SOC precautions. Because the power calculation showed that 3650 catheter-days were required, 1 interim analysis was planned. This analysis showed that the chance of finding a 50% difference between groups would have been <1.5% if the trial had been continued until predefined recruitment numbers were attained. Therefore, the study was discontinued. One might argue that we can only draw conclusions about AC colonization. However, a good correlation between the incidence of catheter-tip colonization and CRBSI has recently been reported elsewhere [11]. Furthermore, it is unlikely that a randomized, controlled trial with sufficient power to show a 50% reduction in CRBSIs will ever be performed. Such a study ($\alpha = 0.05$; power, 80%; 1 sided; dropout rate, 20%) would require 2 groups of ~1100 persons with catheters (9000 catheter-days) each. However, we agree that definite conclusions are rarely, if ever, justifiable after only one randomized controlled trial; therefore, future studies would still be very relevant. It would be especially interesting to focus more specifically on AC insertion site infections, because a lower—but nonsignificant (P = .11)—incidence was found for the SBP group.

In this study, the vortex-sonication method for performing catheter-tip cultures was used. This technique allows one to culture the inside and the outside of the tip at the same time. In the study population, the ACs were left in place for an average of 8.6 days, and, in 90 patients, they were left in place for ≥ 10 days. Use of the roll-plate method in a context in which intraluminal catheter tip colonization cannot be neglected could have

led to false-negative catheter-tip culture results and, therefore, underdiagnosis of AC-related bloodstream infections. This is why the vortex-sonication method was chosen.

The need for informed consent was waived by the institutional review board, so all patients who received a new radial or dorsalis pedis AC were enrolled in the study. For this reason, selection bias was avoided, and the external validity of the study results (for catheters in those positions and those inserted without a guidewire) should therefore be good. As mentioned above, for a relatively large proportion of randomized patients, no catheter-tip culture data were available, and this occurred for several reasons. Fifty-one of these patients dropped out as a consequence of gross contamination during accidental removal (e.g., removal by an agitated patient). This probably happens much more frequently for catheters that are inserted distally in a limb (e.g., radial artery catheters) than for longer catheters (e.g., subclavian CVCs) that are inserted in a more central position. There were multiple other reasons for dropping out: for example, transfer of the patient to another hospital or ward, or sometimes (for human reasons, such as absentmindedness) tip culture was just not performed. We tried to prevent these losses as much as possible (e.g., after insertion, all arterial lines were marked with a red label reminding nurses and physicians of the study). When we compared baseline data for the patients who dropped out with data for the analyzable patients and the proportion of patients in each study group who dropped out of the study, we found no differences (P > .1); therefore, we are convinced that the study results remain unbiased, because patients dropped out of the study randomly.

A second aim of this study was to get a better estimate of the incidence of AC colonization and infection in the ICU. Two small observational studies that used standardized catheter culture techniques suggested that AC colonization (20–30 cases per 1000 catheter-days) and infection (3–13 cases per 1000 catheter-days) might be as common as short-term CVC infection and colonization [5, 6]. When data for all patients (both in the randomized and observational studies) who were admitted to our ICU during the study period (figure 1) were considered together, the incidence of catheter infection of any kind was 3.2 cases per 1000 catheter-days.

Although obtaining peripheral blood samples for culture from patients with a new sepsis syndrome is strongly encouraged in our unit, it was rarely successfully performed for the patients included in this study who subsequently had CRBSI diagnosed. These 5 patients were severely ill and had already been hospitalized in the ICU for a very long time. This made obtaining peripheral blood samples very difficult. For 4 of these 5 patients, the results of several cultures of blood samples obtained at different times were positive. In all 5 patients, sepsis disappeared ≤ 48 h after catheter removal. This strongly suggests that the patients really had arterial CRBSI. Furthermore,

the positive predictive values for cultures of blood samples obtained through the AC were recently shown to be exactly the same as the values for blood samples obtained by peripheral venipuncture [12].

In a systematic review of all papers published during 1990–2002 about short-term CVC-related infection (29 clinical studies that included data on 94,595 catheter-days, 1281 colonized catheters, and 259 CRBSIs), the respective mean incidences of catheter-tip colonization and CRBSI were 13.5 and 2.7 cases per 1000 catheter-days [11]. This incidence is comparable to the incidence we found for ACs. This finding is not unexpected. ACs are used for obtaining blood samples several times per day, and, sometimes, for the most severely ill patients, samples are obtained every few hours. Therefore, hub contamination as the portal of entry of catheter colonization and infection is one of the possible causes. An extraluminal route of infection (migration of bacteria from the skin around the insertion site to the catheter tip) is another likely explanation. With regard to the latter route of infection, a randomized trial recently showed the usefulness of a chlorhexidine sponge (Biopatch; Johnson & Johnson Medical) placed around the insertion site of the catheter for the prevention of catheter-related infection. With use of this method, the incidence of colonization of CVCs and ACs was reduced significantly [13].

Because the frequency of colonization and infection of ACs was high in this study, other measures to prevent AC infection need to be developed. Antimicrobial- or antiseptic-coated catheters have been shown to decrease CVC-related infectious complications. The same techniques may be useful for ACs, but randomized, controlled trials will have to confirm this. Investigation of a means to protect the insertion site of the catheter and the hub during manipulation should be part of the way forward.

Unlike the findings for CVC-related colonization and infection, this study did not show a reduction in the rate of AC colonization when SBPs were used during insertion of arterial catheters in the radial or dorsalis pedis artery without the use of a guidewire. The incidence of AC colonization and infection seems to be similar to the incidence for CVCs.

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