# Prospective Randomized Trial of 10% Povidone-Iodine versus 0.5% Tincture of Chlorhexidine as Cutaneous Antisepsis for Prevention of Central Venous Catheter Infection

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**A multicenter prospective, randomized, controlled trial, with 0.5% tincture of chlorhexidene versus 10% povidone-iodine as cutaneous antisepsis for central venous catheter (CVC) insertion, was conducted for patients in intensive care units. Of 374 patients, 242 had a CVC inserted for >3 days and were used for the primary analysis. Outcomes included catheter-related bacteremia, significant catheter colonization (≥15 colony-forming units [cfu]), exit-site infection, serial quantitative exit-site culture (every 72 h), and molecular subtyping of all isolates. Patients in both study groups were comparable with respect to age, sex, underlying disease, length of hospitalization, reason for line insertion, and baseline APACHE II score. Documented catheter-related bacteremia rates were 4.6 cases per 1000 catheter-days in the chlorhexidine group ($n = 125$) and 4.1 cases per 1000 catheter-days in the povidone-iodine group ($n = 117$; not significant [NS]). Significant catheter-tip colonization occurred in 24 (27%) of 88 patients in the povidone-iodine group and in 31 (34%) of 92 patients in the chlorhexidine group (NS). A mean exit-site colony count of $5.9 \times 10^5$ cfu/mL per 25 cm$^2$ of the surface area of skin in the povidone-iodine group versus $3.1 \times 10^5$ cfu/mL per 25 cm$^2$ in the chlorhexidine group (NS) was found. There was a trend toward fewer exit-site infections in the chlorhexidine group (0 of 125 patients) versus those in the povidone-iodine group (4 of 117 patients; $P = .053$). Results of an intention-to-treat analysis were unchanged from the primary analysis. No difference was demonstrable between 0.5% tincture of chlorhexidine and 10% povidone-iodine when used for cutaneous antisepsis for CVC insertion in patients in the intensive care unit.**

Catheter-related bacteremia is the most frequent serious complication related to the use of central venous catheters (CVCs) [1–3]. Rates of catheter-related bacteremia in intensive care units (ICUs) are 2.1–30.2 cases per 1000 catheter-days (median, 23.7 per 1000 catheter-days), depending on the type of ICU [4]. Although infections may occur because of infusate contamination [5] or hub colonization with contiguous intraluminal spread [6], the majority of infections are likely secondary to invasion of the transcutaneous insertion tract by microorganisms from the patient's own skin flora [7, 8]. Studies that used molecular subtyping methods have confirmed the correlation between organisms isolated in cases of catheter-related bacteremia and the patient's pericatheter skin flora [9, 10].

Because the pathogenesis of the majority of central catheter–related infections relates to microorganism invasion from the insertion site, the use of agents for cutaneous antisepsis at the time of line insertion and for subsequent catheter care is regarded as one of the most important measures for prevention of these infections. The optimal agent for cutaneous antisepsis is unknown, but many different types of agents have been used, including iodophors such as 10% povidone-iodine, tincture of iodine, aqueous chlorhexidine, tincture of chlorhexidine, triclosan, and 70% isopropyl alcohol. Chlorhexidine is a potent germicide that has been widely used for hand washing, skin disinfection, oral care, and topical treatment of burns and surgical wounds. Aqueous chlorhexidine as a hand washing agent has been found to be superior to nonmedicated soaps and iodophors for removal of microorganisms from the hands of health care workers [11, 12]. Two published randomized controlled trials [13, 14] comparing different agents for cutaneous antisepsis in critical care populations have suggested that chlorhexidine-containing preparations may be superior to povidone-iodine for

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prevention of local catheter infections and catheter-related sepsis associated with CVCs.

To determine which solution is the most effective for preventing CVC exit-site colonization, significant catheter-tip colonization, and catheter-related bacteremia in ICU patients, we performed a multicenter prospective randomized trial comparing 10% povidone-iodine versus 0.5% tincture of chlorhexidine solution for cutaneous antisepsis during CVC insertion and for subsequent line care.

## Patients and Methods

*Patients.* Our study was conducted at 3 university medical school–affiliated teaching hospitals, which included 2 medical-surgical ICUs, 1 medical ICU, and 1 neurosurgical ICU; these 3 sites had a total of 55 beds. All patients >18 years of age who had CVCs inserted for any purpose were eligible for inclusion in the study, provided the treating physician felt the inserted catheter would be present for a minimum of 72 h. This eligibility criterion increased the opportunity of finding catheter-related infections [15–17]. The study was approved by the Institutional Review Board, and written informed consent was obtained from all patients or from their surrogate decision maker.

*Study design.* By use of a blinded block randomization schedule, patients were assigned to either 10% povidone-iodine (Purdue Frederick, Pickering, Ontario, Canada) or 0.5% tincture of chlorhexidine (Medi-Flex, Overland Park, KS) as the agent for initial and subsequent cutaneous antisepsis for catheter care. The CVCs consisted of conventional single- or multilumen polyurethane catheters, silicone catheters, and pulmonary arterial catheters. Femoral venous catheters, peripheral arterial catheters, and peripheral venous catheters, including peripherally inserted central catheters, were not included in the study. The site for central venous cannulation was prepared with the appropriate agent and allowed to dry according to a standardized protocol. All catheters were inserted by surgical or medical staff who used maximal barrier precautions with sterile gloves, gown, mask, and large drapes. No silver antiseptic or antimicrobial-impregnated catheters were allowed for patients enrolled in the study. All catheters were cared for in a similar manner. Sterile gauze dressings were changed every 72 h or sooner if soiled or wet, and the catheter exit site was cleansed for 20–30 s with the agent to which the patient had been randomized. The insertion site was inspected every 72 h for evidence of infection, including erythema and purulent discharge at the exit site. Decisions to remove catheters were made independently by the treating physicians.

*Bacteriologic methods.* Before the catheter was removed, the catheter entry site was cleansed with the antiseptic solution to which the patient had been randomized, to prevent potential contamination by bacteria located at the cutaneous exit-site surface but not in the subcutaneous tunnel. Following removal, a 2-cm segment of the distal catheter tip was cultured by use of semiquantitative techniques [18]. All isolates were identified by use of standard methods [19]. Isolates were further characterized by susceptibility testing [20] and with molecular subtyping with pulsed-field gel electrophoresis (PFGE) [21]. Organisms with identical DNA profiles isolated from the colonized catheter tip and from the bloodstream were considered to provide confirmation of the diagnosis of catheter-related sepsis. Quantitative exit-site cultures were performed at each dressing change. A 5-by-5–cm template was placed over the catheter insertion site, and a sterile cotton-tipped applicator moistened with 0.01 *M* PBS was used to culture the surface of the skin. We used 2 sets of back-and-forth strokes, with the second set perpendicular to the first [10]. The applicators were then transferred to sterile tubes containing trypticase soy broth and cultured quantitatively.

*Definitions.* Definite catheter-related bacteremia was diagnosed in patients with a single positive blood culture, with no other source of bacteremia, in the presence of a culture of a catheter segment from which the same organism was isolated, as confirmed by molecular subtyping. If results of molecular subtyping were discordant, patients were considered to have bacteremia from a source other than the line. Probable catheter-related sepsis was defined on the basis of $\geq 2$ positive blood cultures (or a single positive blood culture for *Staphylococcus aureus*) from a patient with clinical and microbiologic data disclosing no other source for the bacteremia except the intravascular device but with no catheter tip available for culture. Significant catheter-tip colonization (local catheter infection) was defined as the growth of $\geq 15$ cfu from a semiquantitative culture of the catheter tip by the roll-plate technique [18]. Exit-site infection was defined as purulent discharge at the exit site, regardless of whether an organism was cultured from the site.

*Statistical analysis.* Baseline characteristics (age, sex, APACHE II score, host factors including surgery, trauma, renal failure, corticosteroid use, diabetes mellitus, or underlying malignancy, and presence of other devices, including endotracheal tubes, tracheostomy, or other central catheters) of the 2 groups were compared with the $\chi^2$ test for categorical data and the Mann-Whitney *U* test for continuous data [22]. Differences were calculated for the categorical outcomes of catheter-related bacteremia, local catheter infection, and purulent exit-site infection between the povidone-iodine and the chlorhexidine groups by $\chi^2$ analysis or by Fisher's exact test. For comparison of significant differences in incidence rates, the exact test [22] for incidence density was used. This was done for evaluable patients who had their CVCs inserted for >72 h and on an intention-to-treat analysis of all enrolled patients. The results of exit-site quantitative cultures were compared by the Mann-Whitney *U* test. Power calculations were based on the primary outcomes of catheter-related bacteremia and local catheter infection. On the basis of findings described in the literature [13, 14], we hypothesized that there would be a 75% RR reduction in both outcomes in patients in the chlorhexidine group. To ensure with 80% power and with 95% confidence that a true difference of this degree would be detected between the 2 groups, 320 and 88 evaluable patients, respectively, would be required in each of the 2 arms of the study. The research team and the physician inserting the CVC could not be blinded to the antiseptic solution used because of the different colors of the 2 solutions (brown for the povidone-iodine and colorless for the chlorhexidine). However, all microbiological techniques were performed by a technologist blinded to the patients' randomization and clinical status.

## Results

*Patient characteristics.* The eligible patient population among the 3 sites was estimated to be 576–768 patients, on the basis of the previous year's admissions, but, because of unforeseen restructuring and administrative changes affecting the ICUs during the course of the study, the number of eligible patients was reduced by an estimated 30%–45%. More than 90% of the patients who were approached agreed to enroll in the study. A total of 374 patients were enrolled (181 in the povidone-iodine group and 193 in the chlorhexidine group) over a 1-year period. Of these patients, 242 had a central line for >72 h (117 in the povidone-iodine group and 125 in the chlorhexidine group), and 132 had their line removed or died before 72 h. The group of 242 patients in whom the central line was inserted for >72 h was used for the primary analysis. An intention-to-treat analysis of all 374 patients was also performed. In the primary analysis, patient characteristics were similar for risk factors predisposing to nosocomial infection (table 1). Patients' APACHE II scores were similar for patients in both groups, reflecting a critically ill patient population. The majority of patients were on mechanical ventilation, and corticosteroid use, renal failure (defined as requiring dialysis), and diabetes (defined as requiring insulin therapy) were common in both groups (table 1). The average length of hospitalization before CVC insertion was similar in patients of both groups.

*Characteristics of catheter insertions.* Catheter insertion characteristics for the primary analysis are described in table 2. The site of catheter insertion was either the internal jugular vein or the subclavian vein, and distribution was similar in patients of both study groups. None of the catheters was placed over a guidewire in a preexisting catheter site. Catheters were left in place a mean (±SD) of 8.3 ± 6.9 days in patients in the povidone-iodine group, compared with a mean (±SD) of 6.9 ± 3.6 days in the patients assigned to the chlorhexidine group ($P = .29$), before removal. The majority of catheters were inserted for purposes of hemodynamic monitoring or fluid resuscitation. The mean number of applications of the cutaneous antisepsis solution at the time of line insertion was 3.5 ± 1.9 for patients in the povidone-iodine group and 3.1 ± 1.2 for those in the chlorhexidine group ($P = .29$).

*Outcomes.* In the analysis of 242 patients who had their catheters in for >72 h, we found that 125 received chlorhexidine and 117 received povidone. Of these, a total of 180 (74%) catheter tips were available for culture. Catheter-related bacteremia in which the catheter-tip organism and the blood culture isolate were identical occurred in 4 (3.4%) of 117 patients (4.1 cases per 1000 catheter-days) in the povidone-iodine group versus 4 (3.2%) of 125 patients (4.6 cases per 1000 catheter-days) in the chlorhexidine group ($P$ = not significant [NS]). Two additional cases of probable catheter-related bacteremia (1 *S. aureus* and 1 coagulase-negative staphylococcus) occurred, but a catheter tip was not recovered to verify the diagnosis. One of these patients had received chlorhexidine and the other povidone. Local catheter infection (colonization of ⩾15 cfu) occurred in 55 (30.6%) of 180 patients. The rate of local catheter infections was similar among the patients in the povidone-iodine group versus those in the chlorhexidine group (24 [27%] of 88 [46 cases per 1000 catheter-days] vs. 31 [34%] of 92 [34 cases per 1000 catheter-days], respectively; $P$ = NS). Mean exit-site quantitative cultures were not significantly different in the 2 groups (table 3). There were no purulent exit-site infections in patients in the chlorhexidine group, compared with 4 (3.4%) of 117 patients in the povidone-iodine group ($P = .053$).

**Table 1.** Underlying characteristics of patients assigned to chlorhexidine-treated vs. povidone-iodine–treated groups.

| Characteristic | 0.5% Chlorhexidine ($n$ = 125) | 10% Povidone-iodine ($n$ = 117) | $P$[a] |
|---|---|---|---|
| Age, in years, mean ± SD | 58.3 ± 16.8 | 62.2 ± 16.0 | .08 |
| Sex, male:female | 78:47 | 72:45 | NS |
| APACHE II score | 21.2 ± 8.9 | 19.7 ± 8.1 | .19 |
| Host factor | | | |
| Postsurgery | 48 (38.4) | 53 (45.3) | NS |
| Trauma | 2 (1.6) | 3 (7.6) | NS |
| Renal failure | 26 (20.8) | 22 (18.8) | NS |
| Corticosteroids | 34 (29.2) | 35 (29.9) | NS |
| Diabetes | 20 (16.0) | 21 (17.9) | NS |
| Cancer | 30 (24.0) | 18 (15.4) | .09 |
| Other device | | | |
| Endotracheal tube | 97 (77.6) | 89 (76.1) | NS |
| Tracheostomy | 4 (3.2) | 4 (3.4) | NS |
| Other central line | 25 (20.0) | 30 (25.6) | NS |

NOTE. All data are no. (%) unless indicated otherwise. NS, not significant.
[a] Values of $P < .20$ are shown.

Organisms isolated from patients with catheter-related bacteremia and local catheter infection are shown in table 4. Of the 8 patients with catheter-related bacteremia, PFGE of the blood and catheter-tip isolates revealed identical patterns in 5 patients and a closely related (1 band difference) pattern in 2 patients. PFGE was not performed on one of the isolates, but identical antibiograms and biochemical markers were present for the blood and catheter-tip organisms. In one patient, line tip and blood culture isolates (which were from the same species) were completely unrelated by PFGE. This patient was considered to have bacteremia from a source unrelated to the line. Secondary bacteremia (from a source other than a CVC) occurred in 13 (11.1%) of 117 povidone-iodine–treated patients and 22 (17.6%) of 125 chlorhexidine-treated patients ($P$ = .21).

*Intention-to-treat analysis.* The intention-to-treat analysis included 132 additional patients from whom consent was obtained but whose central line was inserted for <72 h or who died before that time. These 132 patients were not significantly different from the remaining 242 patients with respect to age, baseline APACHE II score, comorbid conditions, and reasons for catheter insertion (data not shown). Patients who were excluded had been hospitalized a shorter time before enrollment

**Table 2.** Characteristics of central venous catheters in patients assigned to chlorhexidine-treated vs. povidone-iodine–treated groups.

| Characteristic | 0.5% Chlorhexidine ($n$ = 125) | 10% Povidone-iodine ($n$ = 117) | $P$[a] |
|---|---|---|---|
| Site of insertion | | | |
| Jugular | 91 (72.8) | 74 (63.2) | .11 |
| Subclavian | 34 (27.2) | 43 (36.8) | .11 |
| Reason for insertion | | | |
| Hemodynamics | 23 (18.4) | 26 (22.2) | NS |
| Fluids | 101 (80.8) | 90 (76.9) | NS |
| Other | 1 (0.8) | 1 (0.9) | NS |
| Hospital-day catheter inserted, mean ± SD | 16.8 ± 26.5 | 21.1 ± 34.4 | NS |
| Difficult insertion | 3 (2.4) | 7 (6.0) | NS |
| No. of days catheter in place, mean ± SD | 6.9 ± 3.6 | 8.3 ± 7.8 | NS |

NOTE. Data are no. (%) unless indicated otherwise. NS, not significant.
[a] Values of $P < .20$ are shown.

in the study—21.1 (±31.5 SD) versus 5.9 (±17.4 SD) days ($P < .001$). Of 374 patients, povidone was used in 181 patients and chlorhexidine in 193 patients for cutaneous antisepsis. Baseline patient and catheter insertion characteristics were not significantly different in the 2 groups. A single additional case of catheter-related bacteremia due to *Pseudomonas aeruginosa* occurred in a patient treated with povidone-iodine. The rate of catheter-related bacteremia was 4.4 cases per 1000 catheter-days (5 [2.8%] of 181) in the povidone-iodine group versus 3.9 cases per 1000 catheter-days (4 [2.1%] of 193) in the chlorhexidine group ($P$ = NS). No additional purulent exit-site infections occurred in the remaining 132 patients. A total of 232 catheter tips were available for culture (116 in each group). Local catheter infection occurred in 27 (23%) of 116 patients in the povidone arm and in 36 (31%) of 116 patients in the chlorhexidine group ($P$ = .18). Overall, the results of the intention-to-treat analysis were unchanged from the primary analysis.

## Discussion

In our study, we compared a 0.5% tincture of chlorhexidine solution with a 10% povidone-iodine solution for cutaneous antisepsis to prevent CVC-related bacteremia. We could not document a difference in rates of catheter-related bacteremia (with an identical catheter-tip isolate) between patients in the 2 treatment arms (4.6 cases per 1000 catheter-days in patients in the chlorhexidine group and 4.1 cases per 1000 catheter-days in the patients in the povidone-iodine group; $P$ = NS). However, because of a lower-than-anticipated enrollment, our study lacked sufficient power to demonstrate this difference. Significant catheter-tip colonization or local catheter infection (⩾15 cfu) occurred in 27% of patients (46 cases per 1000 catheter-days) in the povidone-iodine group and 34% of patients (34 cases per 1000 catheter-days) in the chlorhexidine arm ($P$ = NS). Exit-site quantitative cultures taken every 72 h by use of a standard template also demonstrated no difference in patients' mean colony counts between the 2 treatment arms. The only difference appeared to be a trend toward fewer purulent exit-site infections in the chlorhexidine group (0 of 125 patients) versus the povidone-iodine group (4 of 117 patients; $P$ = .053). Overall, there appeared to be little difference between chlorhexidine and povidone-iodine used for cutaneous antisepsis during line insertion.

Our findings differ from previously published randomized controlled trials comparing different solutions for cutaneous antisepsis in this patient population [13, 14]. Maki et al. [13] compared 10% povidone-iodine, 70% alcohol, and a 2% aqueous chlorhexidine solution for cutaneous antisepsis. The patients in the chlorhexidine arm of this study were found to have a significantly lower rate of local catheter infection and catheter-related bacteremia. There were several key differences between the study by Maki et al. and our study. First, the majority of catheters in the study by Maki et al. were arterial lines, with only 67 chlorhexidine-treated central lines and 77 povidone-iodine–treated central lines studied. The rate of catheter-related bacteremia for only CVCs in this study do not significantly differ for patients in the chlorhexidine group (1 [1.5%] of 67; 2.8 cases per 1000 catheter-days) versus patients in the povidone-iodine group (5 [6.5%] of 77; 12.3 cases per 1000 catheter-days). Arterial catheters and CVCs may behave differently with

**Table 3.** Outcome measurements in patients assigned to chlorhexidine-treated vs. povidone-iodine–treated groups.

| Outcome | 0.5% Chlorhexidine ($n$ = 125) | 10% Povidone-iodine ($n$ = 117) | $P$[a] |
|---|---|---|---|
| Local catheter infection, ⩾15 cfu | | | |
| No. infected patients/total patients (%) | 31/92 (34) | 24/88 (27) | NS |
| No. per 1000 catheter-days | 34 | 46 | NS |
| Catheter-related bacteremia | | | |
| No. infected patients/total patients (%) | 4/125 (3.2) | 4/117 (3.4) | NS |
| No. per 1000 catheter-days | 4.6 | 4.1 | NS |
| Exit-site quantitative culture, mean ± SE, $\times 10^5$ cfu/mL per 25 cm$^2$ | 3.1 ± 1.9 | 5.9 ± 2.6 | NS |
| Purulent exit-site infections | | | |
| No. infected patients/total patients (%) | 0/125 (0) | 4/117 (3.4) | .053 |
| No. per 1000 catheter-days | 0 | 4.1 | .15 |

NOTE. NS, not significant.
[a] Values of $P < .20$ are shown.

**Table 4.** Microorganisms from patients with catheter-related bacteremia and significant catheter colonization (local catheter infection).

| Organism | 0.5% Chlorhexidine ($n$ = 125) | | 10% Povidone-iodine ($n$ = 117) | |
|---|---|---|---|---|
| | Catheter-related bacteremia | Local catheter infection, ⩾15 cfu | Catheter-related bacteremia | Local catheter infection, ⩾15 cfu |
| Coagulase-negative staphylococci | 2 | 23 | 3 | 14 |
| *Staphylococcus aureus* | 2 | 1 | 1 | 3 |
| *Enterococcus* species | 0 | 1 | 0 | 1 |
| Enterobacteriaceae | 0 | 5 | 0 | 6 |
| *Pseudomonas* species | 0 | 1 | 0 | 0 |

respect to the development of catheter-related sepsis. Also, 20%–24% of central catheters were inserted in "old" sites over a guidewire, a practice that is likely associated with a higher risk of catheter-related sepsis [23, 24]. We chose to study a more homogenous population of only centrally placed venous catheters inserted in fresh sites.

Mimoz et al. [14] demonstrated a significant reduction in catheter colonization and in catheter-related sepsis with use of a solution containing 0.25% chlorhexidine, 0.025% benzalkonium chloride, and 4% benzyl alcohol versus a 10% povidone-iodine solution. However, significant catheter colonization (i.e., local catheter infection) was defined as a quantitative culture of a catheter tip showing $\geqslant 1 \times 10^3$ cfu/mL. We used a definition of ⩾15 cfu as indicative of significant local catheter infection. This was based on the semiquantitative culture results reported by Maki et al. [18], which demonstrated this level of local catheter-tip organism growth to be a major risk factor for catheter-related bacteremia. Also, the presence of bacteremia was not included in their definition of catheter-related sepsis, which was instead defined on the basis of resolution of fever within 48 h of catheter removal. The rate of bacteremic catheter-related sepsis was in fact the same in both treatment groups (3 and 4 cases per 1000 catheter-days), which was similar to the rate observed in our study. In addition, we performed PFGE to ensure that the catheter-tip organism and bloodstream isolate were identical, further confirming the diagnosis of catheter-related sepsis. We feel that, in a complex ICU patient population, strict definitions are important to ensure that patients are not falsely classified as having catheter-related sepsis.

In addition to differences in patient populations, differences in types of chlorhexidine-containing antiseptic compounds may account in part for the lack of superior effect for chlorhexidine observed in our study. We used a 0.5% tincture of chlorhexidine solution, compared with a 2% aqueous solution used by Maki et al. [13]. However, the concentration of chlorhexidine in our solution was 5000 $\mu$g/mL, which is still 100-fold higher than the MICs against most nosocomial bacteria and yeast [13]. Mimoz et al. [14] used a commercially available 0.025% chlorhexidine solution, but it also contained 4% alcohol and 0.025% benzalkonium chloride. The latter compound has been shown to have synergistic in vitro activity when used in combination with chlorhexidine [25].

The microbes recovered from colonized catheter tips and from patients with catheter sepsis consisted primarily of coagulase-negative staphylococci, *S. aureus,* and enteric gram-negative organisms. Studies performed in ICUs have noted a similar distribution of organisms responsible for catheter-related sepsis [26, 27]. Chlorhexidine has been proposed to be superior to povidone at eradication of gram-positive cocci, and a study has demonstrated the superiority of chlorhexidine for eradication of coagulase-negative staphylococci at peritoneal dialysis catheter exit sites [28]. However, the rate of catheter-tip colonization or sepsis due to coagulase-negative staphylococci was not different in our study (chlorhexidine, 24 of 125 catheters, vs. povidone, 17 of 117 catheters), with a trend favoring povidone-iodine. We were not able to demonstrate any clear benefit for decreasing infection attributable to any particular subgroup of organisms with use of either antiseptic solution.

Our study did have several limitations. The study was designed to include only patients in whom a central line was likely to be inserted for >72 h. Previous data suggested that such patients could be determined >90% of the time before line insertion [29]. However, 35% of enrolled patients in our study had a central line inserted for <72 h and were excluded from the primary analysis. However, this finding is unlikely to have biased the results, because excluded patients were divided equally among the 2 treatment arms, and an intention-to-treat analysis of all 374 patients did not alter the overall results. Also, 25% of catheter tips were not recovered in both groups at the time of catheter removal. However, catheter-related sepsis was suspected clinically in only 2 of these patients (1 in each treatment arm). Therefore, comparative rates of catheter-related bacteremia in the 2 groups would not have been affected. There also may have been a selection bias, because the sickest patients (i.e., those who were unconscious or intubated) may not have been approached for consent. This could result in a lower-than-expected rate of catheter-related infections. To minimize this potential bias, consent was obtained from a patient surrogate if the patient was unable to give informed consent. Also, such a bias would be expected to be equally distributed among the 2 study arms because of the randomization process.

As noted previously, because of lower-than-expected patient recruitment, our study did not have sufficient power to detect a difference in catheter-related bacteremia rates. Because the rate of catheter-related bacteremia and patient recruitment was

lower than expected, our study only had a 15% power to demonstrate a difference in this outcome (20% power in intention-to-treat analysis). However, the study did have sufficient power to detect differences in rates of local catheter infection between the 2 treatment arms. On the basis of the rates of local catheter infection that we expected, our study had a 95% power to detect a significant difference for this outcome in the primary analysis and a 97% power in the intention-to-treat analysis.

It is possible, however, that our findings demonstrate that no true differences exist in any of the outcomes of catheter-related infection, whether chlorhexidine or povidone-iodine is used as cutaneous antisepsis in this setting. The rates for catheter-related bacteremia were similar to those described by Mimoz et al. [14] and Maki et al. [13] when similar populations were compared. It is noteworthy that, when similar patients from all 3 randomized controlled studies are combined, the rates of bacteremia are 7 of 279 (2.5%; 3.9 cases per 1000 catheter-days) and 11 of 265 (4.2%; 5.9 cases per 1000 catheter-days) for patients in the chlorhexidine and povidone-iodine groups, respectively ($P$ = NS). With the combined results, the statistical power to detect a trend favoring chlorhexidine with an $\alpha$ of 0.1 is 80%. Similarly, the rates of significant catheter colonization between the 2 groups for the combined results for the 3 studies reveal no significant differences (17% and 22.4%), which would normally be a more sensitive indicator than that of catheter-related bacteremia. The degree of mean exit-site colonization between the 2 groups was also similar in our study and that of Maki et al. [13], suggesting that the degree of exit-site colonization would not account for any observed differences between the 2 groups

Strengths of our study include the use of strict microbiological criteria for catheter-related bacteremia with confirmation by molecular techniques. Therefore, although the study was not conducted in a blinded manner, the use of strictly defined end points should have minimized any possible biases. Also, exclusion of peripheral arterial lines, peripherally inserted central venous lines, and catheters placed over guidewires allowed for a more homogenous study sample.

In summary, we were not able to demonstrate a significant difference between chlorhexidine and povidone-iodine for prevention of catheter-related bacteremia when either solution was used for cutaneous antisepsis during CVC insertion and for subsequent catheter care. This is contrary to previously published studies examining this issue, but our study, conducted in a more homogeneous population, suggests that the 2 products examined are similar and provides further evidence that products containing chlorhexidine, including the 0.5% tincture product, do not have a disadvantage, compared with 10% povidone, when used as a cutaneous antiseptic in an ICU population.

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