Inflammation at the insertion site is not predictive of catheter-related bloodstream infection with short-term, noncuffed central venous catheters

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Background: Noncuffed, percutaneously inserted central venous catheters (CVCs) are widely used and cause at least 250,000 bloodstream infections (BSIs) in U.S. hospitals each year. We report a prospective study to determine whether inflammation at the insertion site is predictive of CVC-related BSI.

Methods: Percutaneously inserted, noncuffed CVCs inserted into the subclavian, internal jugular, or femoral vein in two randomized trials during 1998–2000 were prospectively studied; most patients were in an intensive care unit. The condition of the insertion site was evaluated daily by research nurses, quantifying pain (0, 1), erythema (0–2), swelling (0, 1), and purulence (0, 1); the lowest possible overall inflammation score was 0 and the highest was 5. CVC-related BSI was confirmed in each case by demonstrating concordance between isolates from the catheter segment and from blood cultures by restriction-fragment DNA subtyping.

Results: Among 1,263 CVCs prospectively studied, 333 (26.3%) were colonized at removal; of these, 35 catheters (2.7%) caused BSIs (5.9 per 1,000 CVC days), BSIs were caused by coagulase-negative staphylococci (n = 27), enterococci (n = 4), enteric Gram-negative bacilli (n = 3), or Candida (n = 1). Most insertion sites showed little or no inflammation at the time of removal. There were no significant differences among mean scores for each inflammatory variable examined or overall score among colonized CVCs (0.1 ± 0.1), catheters causing CVC-related BSI (0.1 ± 0.1), and noncolonized CVCs (0.1 ± 0.1). The sensitivity of local inflammation for diagnosis of CVC-related BSI was dismal (0–3%).

Conclusion: Local inflammation is uncommon with infected CVCs, probably because most catheter-associated infections are currently caused by coagulase-negative staphylococci, a pathogen that incites little local or systemic inflammation. Whereas overt inflammation of the insertion site should raise suspicion of CVC-related BSI caused by Staphylococcus aureus or Gram-negative bacilli, especially if the patient has fever or other signs of sepsis, in general, site appearance cannot be relied on to identify catheter colonization or CVC-related BSI. (Crit Care Med 2002; 30:2632–2635)

Key Words: central venous catheter; noncuffed; percutaneously inserted; bloodstream infection

Safe and reliable vascular access is an essential component of modern-day health care. However, the devices used for vascular access are associated with a substantial risk of bloodstream infection (BSI) (1–3). It is estimated that at least 250,000 intravascular device-related infections occur in the United States each year (1), each associated with a 20–25% attributable mortality (4–7) and prolonged hospitalization (5–9). The majority of BSIs related to intravascular access are caused by central venous catheters (CVCs) of various types (1–3), especially noncuffed catheters inserted in the internal jugular, subclavian, or femoral vein and used for short-term or intermediate-term access.

Numerous risk factors—host-related and catheter-related factors—that predispose to CVC-related BSI have been identified in prospective studies (1–3). However, few studies have examined clinical predictors for the presence of CVC-related BSI (10–12). We report a prospective study undertaken to determine whether pain, swelling, erythema, or purulence at the insertion site is predictive of catheter-related infection with noncuffed CVCs.

METHODS

Patients participating in two randomized trials during 1998–2000, one evaluating the efficacy of a novel chlorhexidine-gluconate-impregnated sponge dressing (13) and the other evaluating 1% tincture of chlorhexidine for prevention of catheter-related infection (14), formed the study population. Data were collected prospectively on study patients with newly inserted CVCs, including demographic features, underlying diseases, severity of illness according to Acute Physiology and Chronic Health Evaluation (APACHE) II score (15), reason for placement of the catheter, service, antibiotic use, length of hospital stay, number and sites of all central catheters placed, number of days each catheter was in place, presence of other invasive devices (urinary catheters and endotracheal tubes), and all clinical and laboratory data pertaining to infection.

Each study patient was evaluated daily by a team of research nurses. The patient was asked about discomfort at the insertion site, and the site was visually inspected and scored quantitatively for inflammation. Erythema was scored on a scale of 0 to 2, with 0 representing no erythema, 1 representing slight erythema, and 2 representing florid erythema. Puru-
ence, swelling, and pain were noted to be either absent (score of 0) or present (score of 1). The overall score each day could range from 0 to 5.

Microbiologic Methods. At catheter removal, skin of the insertion site was cultured semiquantitatively, and each hub and catheter segment, a proximal intracutaneous segment, and the tip (both transported in a sterile container), were cultured semiquantitatively, and each hub and fluid aspirated aseptically from the most distal injection port of each lumen was cultured semiquantitatively, as previously described (16). For each catheter, two 5-cm segments, a proximal intracutaneous segment and the tip (both transported in a sterile container), were cultured semiquantitatively, and each hub and fluid aspirated aseptically from the most distal injection port of each lumen was cultured semiquantitatively, as previously described (16).

Microorganisms were identified according to standard criteria (17). When catheter-associated BSI occurred, isolates recovered from the insertion site, catheter segments, infusate, or hubs and blood cultures that seemed similar phenotypically were subtyped by pulse-field gel electrophoresis after digestion of genomic DNA with restriction endonucleases (18).

Definitions. Catheter-tip colonization was defined as a positive semiquantitative culture of an intravascular catheter segment (>15 colony-forming units) and was considered synonymous with local colonization of the catheter (16). Catheter-related BSI was defined as isolation of the same strain from the catheter segment, a hub, or infusate and from one or more blood cultures, as proven by restriction-fragment subtyping (1).

Statistical Methods. The significance of differences between the groups was calculated with Student’s t-test for comparison of means. Sensitivity, specificity, and positive and negative predictive values were calculated for each variable examined or overall inflammatory score between colonized catheters and noncolonized catheters (0.1 ± 0.1), catheters causing CVC-related BSI (0.2 ± 0.4), and noncolonized CVCs (0.1 ± 0.1) (Table 3).

The sensitivity, specificity, and positive and negative predictive value of each variable for predicting BSI or colonization are shown in Table 4. Erythema, pain, swelling, and purulence were rarely present and had very poor sensitivity for predicting BSI.

Recognizing that the database comprised patients who were participating in two randomized trials of novel strategies for prevention of CVC-related BSI, and both strategies were found to reduce the prevalence of catheter colonization and CVC-related BSI (13, 14), the predictive value of inflammatory variables for diagnosis of colonization and CVC-related BSI was analyzed for the pooled control groups of both trials. The prevalence of inflammation was similar (overall, one or more signs in 58 catheters—8%), and mean inflammatory scores were not statistically associated with colonization or BSI and sensitivity, and positive predictive values were yet low (0–3% and 0–2%, respectively).

RESULTS

The majority of 1,098 patients studied were elderly and had one or more underlying diseases (Table 1); the mean APACHE II score was 22. Most patients had a urinary catheter and were mechanically ventilated during the period they had a study CVC.

Complete data were obtained for 1,263 CVCs placed in the 1,098 patients, for a total of 6075 CVC days; 333 catheters (26.3%) were colonized at removal and 35 (2.7%) caused CVC-related BSI, a rate of 5.9 per 1000 CVC days. BSIs were caused by coagulase-negative staphylococci (n = 27), enterococci (n = 4), enteric Gram-negative bacilli (n = 3), or Candida (n = 1) (Table 2).

Most insertion sites showed little or no inflammation at the time of removal. There were no significant differences between mean scores for each inflammatory variable examined or overall inflammatory score between colonized CVCs (0.1 ± 0.1), catheters causing CVC-related BSI (0.2 ± 0.4), and noncolonized CVCs (0.1 ± 0.1) (Table 3).

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DISCUSSION

Three previous studies, two prospective (10, 11) and one retrospective (12), examined the condition of the insertion site as a clinical predictor of CVC-related infection. In a prospective study of 169 CVCs used mainly for parenteral nutrition, Armstrong et al. (10) found that >4 mm of erythema at the insertion site was associated with a three-fold increased risk of catheter colonization (>15 colony-forming units; relative risk, 2.97; p = .06); swelling or tenderness was not predictive of colonization. Unfortunately, the report gives no information on catheter-related BSIs, particularly whether erythema was predictive of BSI.

A prospective study of 1,353 CVCs in a university hospital showed that out of 11 cases of CVC-related BSI, 73% of patients had no signs of local inflammation, and the sensitivity and positive predictive value of local inflammation for identification of CVC-related BSI were 27% and 1.5%, respectively. However, purulence at insertion sites, although rare, was found to be highly predictive of CVC-related BSI in a univariate analysis (relative risk, 27.1; p < .005) (11). Information on the microbial profile of infected CVCs was not reported.

In a retrospective cohort study of 268 CVCs placed in the anteceutibial (n = 95), subclavicular (n = 88), axillary (n = 17), or jugular (n = 40) vein in neonates, only 13 of 54 access sites (24%) showed local inflammation in association with catheter-related BSI (sensitivity, 23%; specificity, 94%) (12).
None of the previous three studies utilized DNA subtyping to corroborate the origin of each presumed catheter-related infection. In our large prospective study, in which every CVC-related BSI was confirmed by DNA subtyping, local inflammation or pain at the insertion site was rarely and not predictive of CVC-related BSI. Similar to the studies by Armstrong et al. (10) and Fallat et al. (12), most of our CVC-related BSIs were caused by coagulase-negative staphylococci, an organism that has been shown to elicit little inflammation compared with Staphylococcus aureus (19). Intraluminal infection accounted for a third of all catheter-related BSIs in our study, and that may also explain why insertion-site inflammatory variables had poor predictive value. Studies of exit-site infection in patients with peritoneal dialysis catheters indicate that the presence of local erythema or drainage cannot predict the presence of peritonitis, especially if the infecting organism is coagulase-negative staphylococcus (20, 21).

Inflammation at the insertion site of infected peripheral intravenous catheters was more common 20–30 yrs ago when S. aureus was the predominant cause of vascular catheter-related BSI (22–25). However, S. aureus and Gram-negative bacilli currently account for only a small proportion of CVC-related BSIs in current clinical practice (26). Whereas overt inflammation of the infection site should raise suspicion of CVC-related BSI caused by S. aureus or Gram-negative bacilli, especially if the patient has fever or other signs of sepsis, in general, site appearance cannot be relied on to identify catheter colonization or CVC-related BSI.

**REFERENCES**

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**Table 3. Inflammation at the insertion site of central venous catheter (CVC) removal with uninfected and infected CVCs**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CVC colonization (n = 894)</th>
<th>CVC-related BSI (n = 35)</th>
<th>Colonized CVCs, n = 333</th>
<th>Uninfected CVCs, n = 561</th>
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<td>Purulence</td>
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<td>99</td>
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<td>73</td>
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</table>

*P* < .05; for all comparisons, *p* < .50.

**Table 4. Sensitivity, specificity, and positive and negative predictive value of inflammation at infection site as a predictor of central venous catheter (CVC)-related colonization and bloodstream infection (BSI)**

<table>
<thead>
<tr>
<th>Parameters</th>
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<th>Specificity, %</th>
<th>Positive Predictive Value, %</th>
<th>Negative Predictive Value, %</th>
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