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Major article

# Efficiency of chlorhexidine–silver sulfadiazine-impregnated venous catheters at subclavian sites

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Central venous catheter
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***Background:*** Cost-effectiveness analyses show that chlorhexidine–silver sulfadiazine (CHSS)-impregnated catheters reduce catheter-related bloodstream infection (CRBSI) and central venous catheter (CVC)-related costs. However, no studies have reported the efficiency of CHSS-impregnated catheters for venous access when the risk of CRBSI is low; for example, at the subclavian site. This study determined the cost of a CVC, diagnosis of CRBSI, and antimicrobial agents to treat CRBSI; we did not consider the cost of increased hospital stay.

***Methods:*** This retrospective study included patients admitted to the intensive care unit at Hospital Universitario de Canarias (Tenerife, Spain) who had a subclavian venous catheter.

***Results:*** Patients with CHSS catheters (n = 353) had a lower incidence density of CRBSI (2.12 vs 0 out of 1,000 catheter-days; $P = .02$) and lower CVC-related cost per catheter-day (3.35 ± 3.75 vs 3.94 ± 9.95; $P = .002$) than those with standard catheters (n = 518). CHSS-impregnated catheters were associated with a lower risk of CRBSI (exact logistic regression) (odds ratio, 0.10; 95% confidence interval, $-\infty$ to 0.667; $P = .008$) than standard catheters when controlling for catheter duration. CHSS-impregnated catheters were also associated with a lower CVC-related cost per catheter day than standard catheters (Poisson regression) (odds ratio, 0.85; 95% confidence interval, 0.001-0.873; $P < .001$).

***Conclusions:*** CHSS-impregnated catheters may be efficient in preventing CRBSI in patients with subclavian venous access.



Critically ill patients who need a central venous catheter (CVC)[1] are exposed to the risk of infectious complications that should be prevented, because catheter-related bloodstream infection (CRBSI) can lead to increased morbidity, mortality, and health care costs.[2-4] Different strategies have been proposed to prevent CRBSI, such as the use of a CVC impregnated with antimicrobial agents. To date, the type of CVC-impregnated catheter studied most frequently is a device impregnated with chlorhexidine–silver sulfadiazine (CHSS).

First-generation CHSS-impregnated catheters (coated with the antimicrobial agent on their outer surface only) reduced the incidence of CRBSI compared with nonimpregnated catheters in a meta-analysis of 11 randomized controlled trials and 2,603 catheters.[5] The second-generation CHSS-impregnated catheters (impregnated on both the external and internal surfaces) were also found to reduce the risk of CRBSI compared with nonimpregnated catheters in a meta-analysis of 3 randomized control trials and 1,176 patients.[6]

In addition, several cost-effectiveness analyses showed that CHSS-impregnated catheters decreased the incidence of CRBSI and CVC-related costs.[6-8] However, these cost-effectiveness analyses were complex to interpret because CVC-related costs included, in addition to the costs of CRBSI diagnosis and treatment with antimicrobial agents, also the cost of increased hospital stay. The mean increase in cost due to CRBSI was approximately $10,000 per patient; however, other studies reported increases of up to $40,000[9] or $71,000[10] as a result of increased hospital stays as long as 20 days.

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We previously determined whether the use of CHSS-impregnated catheters reduced health care costs for venous access associated with a high risk of CRBSI; for example, at femoral and jugular vein sites.[11,12] These analyses included only the cost of CVC, the costs of diagnosis, and antimicrobial treatment of CRBSI, and did not include the costs arising from the increase in hospital stay. We found that the use of CHSS-impregnated catheters reduced CVC-related costs associated with both femoral and jugular venous access sites.[11,12]

We are aware of no studies that reported the efficiency of CHSS-impregnated catheters in venous access with a low risk of CRBSI; for example, access at the subclavian site, which included only the cost of the CVC and the costs of diagnosis and antimicrobial treatment of CRBSI, and excluded the costs associated with increased hospital stay. Our study was thus designed to determine the efficiency of CHSS-impregnated catheters for subclavian venous access independently of the costs associated with longer hospital stays.

We excluded this latter cost factor from our economic analysis because in previous cost-effectiveness analyses, it varied widely across studies. Our focus on the efficiency of CHSS-impregnated catheters excluding hospital stay will potentially facilitate decision making based on the cost and clinical benefits of this type of catheter.

Our new aim in this study was to determine whether the use of CHSS-impregnated catheters is an efficient measure to prevent CRBSI in patients with a venous access site associated with a low risk of CRBSI; that is, subclavian access.[13] We wished to know whether the higher direct economic cost of CHSS catheters might be compensated by subsequent savings resulting from the lower risk of CRBSI and its associated costs, although this risk is comparatively lower in patients whose catheter is inserted at a subclavian access site. In previous studies, we found that the use of CHSS-impregnated catheters was efficient in preventing CRBSI in patients with high-risk venous accesses sites; that is, femoral and jugular access,[11,12] because the higher direct economic cost of this type of catheter is likely to be offset by subsequent savings from the lower incidence of the CRBSI. Thus, the focus of our study lies in the evidence that can be used to decide whether CHSS-impregnated catheters are as efficient in preventing CRBSI in patients with subclavian access as in patients with a catheter at high-risk sites.

## MATERIALS AND METHODS

This was a retrospective study of patients admitted to the intensive care unit of the Hospital Universitario de Canarias (Tenerife, Spain) who received 1 or more subclavian venous catheters. The study was approved by our institutional ethics review board.

The catheters used in this study were standard CVCs without impregnation (Arrow, Arrow, Reading, Pa) and CHSS-impregnated Arrowg+ard Blue CVC (Arrow). The physician responsible for the patient decided which catheter would be used.

We defined CRBSI according to the following criteria[14]: positive blood culture obtained from a peripheral vein, signs of systemic infection (fever, chills, and/or hypotension), no apparent source of bacteremia except the catheter, and catheter-tip colonization (significant growth of a microorganism >15 CFU) with the same organism as found in the blood culture (the same species with identical antimicrobial susceptibility). Catheter tips were cultured with the method described by Maki et al.[15]

The diagnosis of CRBSI was made by an expert panel blinded to the type of catheter used (CHSS or standard). Information about the type of catheter (CHSS-impregnated or standard) was removed before the expert reviewers examined the patients' charts. Three physician specialists in infection control, each with more than 10 years of experience, made the diagnosis of CRBSI.

Microbiologic surveillance was based on cultures of urine, tracheal aspirate, throat flora, and wounds twice weekly during the intensive care unit stay. In addition, we obtained clinical samples when there was suspected infection.

Immediate CVC-related costs included only the cost of CVC, the cultures to diagnose CRBSI, and the antimicrobial agents used to treat CRBSI. Data on the costs of CVC and antimicrobial agents were obtained from the hospital accounts department: each CHSS-impregnated catheter cost €26, and each standard catheter cost €15.

The following variables were recorded for each patient: age, sex, Acute Physiology and Chronic Health Evaluation-II score[16]; admission diagnosis; history of chronic obstructive pulmonary disease, diabetes mellitus, chemotherapeutic agents, steroid agents, hematologic tumor, solid tumor, use of antimicrobial agents, mechanical ventilation, tracheostomy, and paralytic agents; duration of catheter use; type of catheter; and CVC-related costs.

Continuous variables are reported as means and standard deviations, and categorical variables are reported as frequencies and percentages. We compared catheter groups (CHSS-impregnated vs standard) with the Student $t$ test for continuous variables and the Kruskal-Wallis or Jonckheere-Terpstra test for categorical variables.

We used exact logistic regression analysis to calculate the magnitude of the effect of catheter type (CHSS or standard) on the occurrence of CRBSI, controlling for the duration of catheter insertion. We used exact Poisson regression analysis to test whether the type of catheter (CHSS-impregnated vs standard) influenced the CVC-related cost per catheter-day. The magnitude of the effect was expressed as the odds ratio (OR) and 95% confidence interval (CI). Survival analysis was done with catheter duration as the dependent variable, type of catheter (CHSS or standard) as the independent variable, and CRBSI as the event; curves were plotted with the Kaplan-Meier method, and the log-rank test was used to compare distributions of CRBSI-free time between the 2 groups. $P$ values $<.05$ were considered statistically significant.

Statistical analyses were done with SPSS 17.0 (SPSS Inc, Chicago, Ill), LogXact 4.1 (Cytel Co, Cambridge, Mass), and StatXact 5.0.3 (Cytel Co).

## RESULTS

We diagnosed 7 CRBSI in 518 patients with standard catheters during 3,297 days, and no CRBSI in 353 patients with CHSS catheters during 2,743 days. Table 1 compares the findings in patients with standard versus CHSS-impregnated catheters. Patients with CHSS-impregnated catheters had a lower rate of CRBSI (1.4% vs 0%; $P = .03$), lower incidence density of CRBSI (2.12 vs 0 CRBSI per 1,000 catheter-days; $P = .02$), and lower CVC-related cost per catheter-day ($3.35 \pm 3.75$ vs $3.94 \pm 9.95$; $P = .002$) than patients with a standard catheter.

Exact logistic regression analysis showed that CHSS-impregnated catheters were associated with a lower risk of CRBSI (OR, 0.10; 95% CI, $-\infty$ to 0.667; $P = .008$) than standard catheters when controlling for catheter duration (Table 2).

Kaplan-Meier analysis showed than CHSS-impregnated catheters were associated with a longer CRBSI-free time than standard catheters (log-rank, 7.99; $P = .005$) (Fig 1).

Poisson regression analysis showed that CHSS-impregnated catheters were associated with a lower CVC-related cost per catheter-day than standard catheters (OR, 0.85; 95% CI, 0.001-0.873; $P < .001$) (Table 2). The cost total of the 7 CRBSIs was €5,157 and the mean cost per CRBSI was €736 ± €283.

**Table 1**
Characteristics of patients receiving either a clorhexidine–silver sulfadiazine (CHSS)-impregnated or a standard catheter

| | Standard (n = 518) (3,297 d) | CHSS (n = 353) (2,743 d) | *P* value |
|---|---|---|---|
| Age, y | 59.50 ± 16.31 | 60.46 ± 15.23 | .39 |
| Male sex | 323 (62.4) | 236 (66.9) | .20 |
| APACHE-II score | 16.32 ± 8.86 | 17.35 ± 8.40 | .14 |
| Admission diagnostic | | | .50 |
| Cardiac surgery | 48 (9.3) | 31 (8.8) | |
| Cardiology | 55 (10.6) | 40 (11.3) | |
| Respiratory | 96 (18.5) | 76 (21.5) | |
| Digestive | 99 (19.1) | 58 (16.4) | |
| Neurologic | 103 (19.9) | 74 (21.0) | |
| Traumatology | 73 (14.1) | 39 (11.0) | |
| Intoxication | 12 (2.3) | 15 (4.2) | |
| Others | 32 (6.2) | 20 (5.7) | |
| Chronic obstructive pulmonary disease | 64 (12.4) | 52 (14.7) | .31 |
| Diabetes mellitus | 147 (28.4) | 100 (28.3) | .99 |
| Chemotherapeutic agents | 27 (5.2) | 16 (4.5) | .75 |
| Steroid agents | 44 (8.5) | 39 (11.0) | .24 |
| Hematologic tumor | 19 (3.7) | 15 (4.2) | .72 |
| Solid tumor | 56 (10.8) | 41 (11.6) | .74 |
| Use of antimicrobial agents | 489 (94.4) | 326 (92.4) | .26 |
| Use of mechanical ventilation | 410 (79.2) | 292 (82.7) | .22 |
| Use of tracheostomy | 86 (16.6) | 103 (29.2) | <.001 |
| Use of paralytic agents | 56 (10.8) | 45 (12.7) | .39 |
| Duration of the catheter, d | 6.36 ± 5.65 | 7.77 ± 6.40 | .001 |
| CRBSI | 7 (1.4) | 0 | .03 |
| Number of CRBSI/1,000 catheter-days | 2.12 | 0 | .02 |
| CVC-related cost, €/d | 3.94 ± 9.95 | 3.35 ± 3.75 | .002 |

NOTE. Values are presented as mean ± standard deviation or n (%).
*APACHE*, Acute Physiology and Chronic Health Evaluation; *CRBSI*, catheter-related bloodstream infection; *CVC*, central venous catheter.

**Table 2**
Exact logistic regression analysis to estimate the risk of catheter-related bloodstream infection (CRBSI), and Poisson regression analysis to estimate central venous catheter (CVC)-related per-day cost for clorhexidine–silver sulfadiazine (CHSS)-impregnated catheters and standard catheters

| | Odds ratio | 95% confidence interval | *P* value |
|---|---|---|---|
| Exact logistic regression analysis | | | |
| CHSS catheter (Reference category: standard catheter) | 0.10 | −∞ to 0.667 | .008 |
| Duration of catheter insertion, d | 1.18 | 1.096-∞ | <.001 |
| Exact Poisson regression analysis | | | |
| CVC-related per-day cost, € | 0.85 | 0.001-0.873 | <.001 |

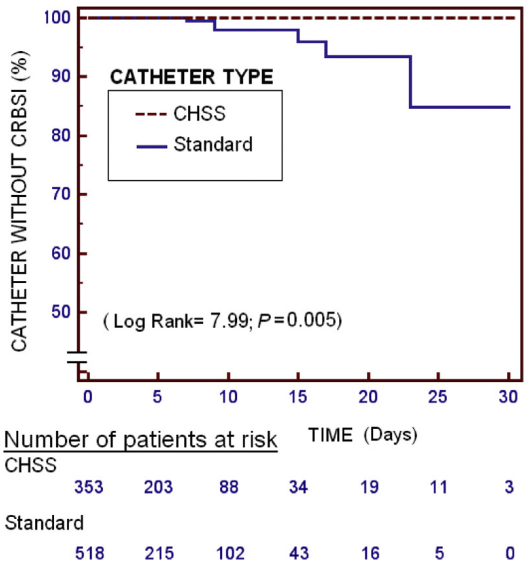


**Fig 1.** Comparison of the distributions of catheter-related bloodstream infection (CRBSI)-free time in patients with subclavian venous access via a clorhexidine–silver sulfadiazine (CHSS)-impregnated or standard catheter.

## DISCUSSION

The novel finding in this study is that the use of a CHSS-impregnated CVC reduced CVC-related costs in patients with a subclavian vein access site. To our knowledge, this is the first study to report data for the comparison of CVC-related costs incurred with CHSS-impregnated versus standard CVC at the subclavian access site. We focused on the cost of the catheter and the costs of diagnosis and treatment of CRBSI, and did not consider other potential costs associated with CRBSI such as increased hospital stay, increased duration of mechanical ventilation, laboratory tests, and other costs.

The results of our study are in consonance with the results of our previous findings that CHSS-impregnated catheters decreased the incidence of CRBSI and the associated CVC-related costs compared with standard catheters used at jugular and femoral vein sites.[11,12] The key point is that the use of CHSS-impregnated CVC may be an efficient measure to prevent CRBSI even in patients with venous access via a site associated with a low risk of CRBSI; for example, the subclavian vein.[13]

We believe that our cost analyses are more straightforward than previous cost-effectiveness analyses,[6-8] and can help in decisions of whether to use a more expensive type of CVC, given that CHSS-impregnated catheters can ultimately save costs and may additionally be an efficient way to prevent CRBSI.

Current guidelines for CRBSI prevention recommend the use of CHSS-impregnated CVC in patients whose catheter is expected to remain in place >5 days, and when the CRBSI rate has not decreased after the implementation of a comprehensive strategy to reduce its occurrence.[17] Allergic reaction to CHSS-impregnated CVCs, although rare, has been reported[18-20]; however, we did not observe any allergic reactions in the patients included in our series.

Another interesting finding of our study was that the duration of catheter insertion was associated with a higher risk of CRBSI. We therefore suggest, as do current guidelines for CRBSI prevention, the removal of the intravascular catheter as soon as it is no longer needed.[17]

Our study has certain limitations. First, the use of CHSS-impregnated or standard catheters was not randomly assigned. Second, this was a single-center study; thus, CVC-related costs may be different at other institutions. However, our study has the strength that the diagnosis of CRBSI was made by an expert panel blinded to the type of catheter (CHSS-impregnated or standard).

## CONCLUSIONS

The use of CHSS-impregnated catheters is an efficient measure to prevent catheter-related bloodstream infection in patients with subclavian venous access.

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