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#### **Major Article**

# Chlorhexidine-silver sulfadiazine-impregnated venous catheters are efficient even at subclavian sites without tracheostomy



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**Background:** Chlorhexidine-silver sulfadiazine (CHSS)-impregnated catheters have been found to decrease the risk of catheter-related bloodstream infection (CRBSI) and central venous catheter (CVC)-related costs. However, there are no published data about cost-effectiveness of the use of CHSS-impregnated catheters in subclavian venous access without the presence of tracheostomy (thus, with a very low risk of CRBSI). That was the objective of this study.

**Methods:** This was a retrospective study of patients admitted to a mixed intensive care unit who underwent placement of subclavian venous catheters without the presence of tracheostomy.

**Results:** Patients with standard catheters (n = 747) showed a higher CRBSI incidence density (0.95 vs 0/1,000 catheter-days; P = .02) and higher CVC-related cost per day (\$3.78 ± \$7.43 vs \$3.31 ± \$2.72; P < .001) than patients with a CHSS-impregnated catheter (n = 879). Exact logistic regression analysis showed that catheter duration (P = .02) and the type of catheter used (P = .01) were associated with the risk of CRBSI. Kaplan-Meier method showed that CHSS-impregnated catheters were associated with more prolonged CRBSI-free time than standard catheters (log-rank = 9.76; P = .002). Poisson regression analysis showed that CHSS-impregnated catheters were associated with a lower central venous catheter-related cost per day than standard catheters (odds ratio, 0.87; 95% confidence interval, 0.001-0.903; P < .001).

**Conclusions:** The use of CHSS-impregnated catheters is an effective and efficient measure for the prevention of CRBSI even at subclavian venous access sites without the presence of tracheostomy.

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Catheter-related bloodstream infection (CRBSI) could lead to an increase in morbidity, mortality, and assistance costs.<sup>1-3</sup> The use of antimicrobial-impregnated central venous catheters (CVCs) has been proposed for the prevention of CRBSI. The antimicrobial agent used for the impregnation of CVCs has been chlorhexidine-silver sulfadiazine (CHSS).<sup>4-7</sup> In a meta-analysis by Veenstra et al,<sup>4</sup> including 2,603 catheters from 11 randomized controlled trials, it was found that first-generation CHSS-impregnated catheters (ie, impregnated only on the external surface) reduced the incidence of CRBSI compared with nonimpregnated catheters. Afterward, in a meta-

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analysis by Hockenhull et al<sup>5</sup> (including 1,176 patients from 3 randomized controlled trials) it was found that second-generation CHSS-impregnated catheters (impregnated on the external and internal surfaces) reduced the risk of CRBSI compared with nonimpregnated catheters.

In addition, some cost-effectiveness analyses have found a reduction on the incidence of CRBSI and CVC-related cost with the use of CHSS-impregnated catheters.<sup>5-7</sup> A limitation of all these cost-effectiveness analyses was that CVC-related cost included the estimated cost that is attributed to the hospital stay increase. Thus, the mean additional cost attributed to CRBSI was approximately \$10,000 per patient, although in some studies the mean additional cost attributed to CRBSI was \$40,0008 and \$71,000.9 To avoid that limitation, our team analyzed the cost-effectiveness of CHSS-impregnated catheters considering only the costs of diagnosis of CRBSI and antimicrobial agents for the treatment of CRBSI, and not including the estimated cost that is attributed to the hospital stay

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increase. We have found that CHSS-impregnated catheters decrease the risk of CRBSI and CVC-related costs in femoral<sup>10,11</sup> and jugular sites,<sup>12</sup> which are venous access sites with high risk of CRBSI.<sup>13,14</sup> Later, we found that CHSS-impregnated catheters decrease the risk of CRBSI- and CVC-related costs for subclavian sites,<sup>15</sup> which is a venous access site with lower risk of CRBSI than femoral and jugular sites.<sup>13,14</sup>

Another issue is that the presence of tracheostomy has been found to be a risk factor for CRBSI at subclavian and jugular venous access sites. <sup>16,17</sup> Those studies included 1,211 and 1,392 catheters, respectively. This association could be due to the fact that respiratory secretions could contaminate more easily a CVC located at subclavian site in the presence of tracheostomy. Now arises the question of whether CHSS-impregnated catheters are also efficient in subclavian venous access without the presence of tracheostomy. To our knowledge, there are no published data about the cost-effectiveness of the use of CHSS-impregnated catheters in subclavian venous access sites without the presence of tracheostomy (thus, with a very low risk of CRBSI).

Thus, the objective of this study was to determine whether the use of CHSS-impregnated catheters could be an effective and efficient measure for CRBSI prevention even in subclavian venous access without the presence of tracheostomy.

#### **MATERIALS AND METHODS**

This retrospective study was carried out in the mixed intensive care unit of the Hospital Universitario de Canarias (Tenerife, Spain). We included patients with subclavian venous catheters without the presence of tracheostomy. The study was approved by the institutional ethic review board.

We used the following CVCs during the study: Arrow (Arrow; Reading, PA), which are standard CVC catheters without impregnation, and ARROWg<sup>+</sup>ard Blue (Arrow), which are CHSS-impregnated catheters (ie, impregnated on the external and internal surfaces). The patient's physician decided the type of CVC for each patient.

We used the following criteria for the definition of CRBSI: signs of systemic infection (eg, fever, chills, and/or hypotension), positive blood culture obtained from a peripheral vein, catheter-tip colonization (significant growth of a microorganism > 15 colony forming units) with the same organism as the blood culture (ie, the same species with identical antimicrobial susceptibility), and no apparent source of bacteremia except the catheter. We used the method described by Maki et al<sup>18</sup> for the culture of each catheter tip.

To calculate CVC-related cost we included only the cost of the CVC, the cost of cultures for diagnosis of CRBSI, and the cost of antimicrobial agents used for the treatment of CRBSI. All data about the costs were obtained from the hospital accounts department. The cost of CVCs was \$17 for standard catheters and \$30 for CHSS-impregnated catheters.

We recorded the following variables for each patient: admission diagnostic, age, acute physiology and chronic health evaluation II score, use of chemotherapeutic agents, presence of chronic obstructive pulmonary disease or diabetes mellitus, duration of the catheter, female sex, presence of a hematologic tumor or solid tumor, use of steroid agents, use of antimicrobial agents, use of mechanical ventilation, use of paralytic agents, type of catheter, presence of CRBSI, and CVC-related cost.

We reported categorical variables as frequencies and percentages, and continuous variables as means and standard deviations. We used Kruskal-Wallis test or Jonckeree-Terpstra test for the comparison of categorical variables, and Student *t* test for the comparison of continuous variables between both catheter groups (CHSS-impregnated or standard catheters).

We used exact logistic regression analysis to determine whether the type of catheter (CHSS or standard) and duration of catheter were associated with the occurrence of CRBSI. Exact nonparametric inference, also known as permutational inference, allowed us to make reliable inferences by exact methods when data were sparse and the accuracy of the corresponding large sample theory was in doubt.<sup>19</sup> We used the exact regression method, so the point estimates, the confidence intervals (including infinite limits), and P values do exist in our study, although the asymptotic ones do not.<sup>20</sup> Poisson regression analysis was carried out to test the influence of the type of catheter (CHSS-impregnated or standard) on the CVCrelated cost per catheter-day. Odds ratio and 95% confidence interval were used to express the magnitude of the effect. We carried out a survival analysis using CRBSI as the event, type of catheter (CHSS or standard) as the independent variable, and catheter duration as the dependent variable. Curves were represented using the Kaplan-Meier method and to compare distributions of CRBSI-free time between groups we used log-rank tests. All P values < .05 were considered statistically significant. We used SPSS 17.0 (IBM-SPSS Inc, Armonk, NY), LogXact 4.1, (Cytel Co, Cambridge, MA), and StatXact 5.0.3 (Cytel Co) for the statistical analysis.

#### **RESULTS**

A total of 214 out of 1,093 CHSS-impregnated catheters (19.6%) and 143 out of 890 standard catheters (16.1%) were located at subclavian venous access sites in the presence of tracheostomy. Table 1 shows the comparison of characteristics of patients with CHSS-impregnated (n = 879) or standard catheters (n = 747) at subclavian venous access sites without the presence of tracheostomy. There were no significant differences between CHSS-impregnated or standard catheters on admission diagnostic, age, acute physiology and chronic health evaluation II score, use of chemotherapeutic agents, presence of chronic obstructive pulmonary disease or diabetes mellitus, female sex, presence of a hematologic tumor, presence of a solid tumor, use of steroid agents, use of antimicrobial agents, use of mechanical ventilation, and use of paralytic agents. We found that

**Table 1**Characteristics of patients receiving chlorhexidine-silver sulfadiazine (CHSS)-impregnated or standard catheter

	CHSS	Standard	
	(n = 879)	(n = 747)	P value
Admission diagnostic			.81
Cardiac surgery	103 (11.7)	80 (10.7)	
Cardiology	92 (10.5)	71 (9.5)	
Respiratory	187 (21.3)	150 (20.1)	
Digestive	171 (19.5)	152 (20.3)	
Neurologic	157 (17.9)	142 (19.0)	
Traumatology	86 (9.8)	80 (10.7)	
Intoxication	33 (3.8)	21 (2.8)	
Others	50 (5.7)	51 (6.8)	
Age (y)	$59.60 \pm 16.47$	$59.54 \pm 16.64$	.94
APACHE II score	$17.06 \pm 7.53$	$16.96 \pm 11.26$	.80
Chemotherapeutic agents	55 (6.3)	45 (6.0)	.92
Chronic obstructive pulmonary disease	110 (12.5)	90 (12.0)	.82
Diabetes mellitus	252 (28.7)	205 (27.4)	.62
Duration of the catheter	$8.95 \pm 4.05$	$5.62 \pm 4.03$	< .001
Female sex	317 (36.1)	274 (36.7)	.84
Hematologic tumor	39 (4.4)	31 (4.1)	.81
Solid tumor	107 (12.2)	89 (11.9)	.88
Steroid agents	101 (11.5)	82 (11.0)	.75
Use of antimicrobial agents	814 (92.6)	698 (93.4)	.56
Use of mechanical ventilation	687 (78.2)	580 (77.6)	.81
Use of paralytic agents	92 (10.5)	68 (9.1)	.40

NOTE. Values are presented as n(%) or mean  $\pm$  standard deviation. *APACHE*, acute physiology and chronic health evaluation.

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