

# The attributable cost, length of hospital stay, and mortality of central line-associated bloodstream infection in intensive care departments in Argentina: A prospective, matched analysis

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**Background:** Limited information is available on the financial impact of central venous catheter-associated bloodstream infection (BSI) in Argentina. To calculate the cost of BSIs in the intensive care department (ICU), a 5-year prospective nested case-control study was undertaken at 3 hospitals in Argentina.

**Methods:** We studied 6 adult ICUs from 3 hospitals. In all, 142 patients with BSI and 142 control patients without BSI were matched for hospital, type of ICU, year of admission, length of stay, sex, age, and average severity of illness score. Patients' length of stay in the ICU was obtained prospectively on daily rounds. The hospitals' finance departments provided the cost of each ICU day. The hospitals' pharmacies provided the cost of antibiotics prescribed for BSIs.

**Results:** The mean extra length of stay for patients with BSI compared with control patients was 11.9 days, the mean extra antibiotic defined daily dose was 22.6, the mean extra antibiotic cost was \$1913, the mean extra cost was \$4888.42, and the excess mortality was 24.6%.

**Conclusions:** In this study, patients with central venous catheter-associated BSI experienced significant prolongation of hospitalization, increased use of health care costs, and a higher attributable mortality. These findings support the need to implement preventative interventions for patients hospitalized with central venous catheters in Argentina. (Am J Infect Control 2003;31:475-80.)

Bloodstream infection (BSI) is an important cause of mortality in patients who are critically ill.<sup>1-9</sup> The most important risk factor for the development of BSI is the central venous catheter (CVC).<sup>4,10-12</sup> Studies have repeatedly demonstrated that CVC-associated BSIs are associated with prolonged hospitalization and increased patient morbidity.<sup>5,13-15</sup> Infection control programs emphasizing improved hand hygiene<sup>16-18</sup> and

catheter care<sup>19-26</sup> in our country and in others have been an important means of reducing CVC-associated BSIs.

Many countries in Latin America, in particular Argentina, lack mandatory infection control programs. As a result, CVC-associated BSIs commonly occur in health care facilities that lack care givers who are familiar with published infection control guidelines.<sup>27</sup>

We report the results of a multicenter nested matched case-control study from a prospective cohort to determine the attributable excess costs with CVC-associated BSIs in patients from 6 cardiac and medical/surgical intensive care departments (ICUs) in 3 medical centers in Argentina.

## METHODS

### Setting

The study was conducted in 3 medical centers in Buenos Aires, Argentina. Each center has an infection control team comprised of an internal medicine doctor with a formal education in infectious diseases and hospital epidemiology, and an infection control nurse.<sup>28</sup>

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Hospital A is a public 250-bed hospital situated in the province of Buenos Aires, Argentina, with 1 medical/surgical ICU (10 beds) and 1 coronary ICU (10 beds). Hospital B is a private 150-bed hospital situated in the province of Buenos Aires, Argentina, with 1 medical/surgical ICU (17 beds) and 1 coronary ICU (15 beds). Hospital C is a private 180-bed hospital situated in the city of Buenos Aires, Argentina, with 1 medical/surgical ICU (10 beds) and 1 coronary ICU (10 beds). All ICUs in the study centers care for patients who have undergone open heart, neurosurgical, and orthopedic operation and patients with complex medical illnesses. The institutional review board at each center approved the study protocol.

### Study population and CVC care practices

All patients admitted to the 3 study ICUs from July 1998 to June 2002 who had a CVC in place for at least 48 hours were included in the study. CVCs were inserted at the bedside by treating physicians who inserted the line after disinfecting the skin with povidone-iodine in hospital A (during the entire study period), hospital B (during 1999), and in hospital C (during 2000). Minimal barriers rather than enhanced barriers (ie, physicians did not wear sterile gowns and gloves and did not use a large sterile drape) were used by health care workers during CVC insertion. Use of enhanced barriers during CVC insertion was incorporated as a standard practice at hospital B between 2000 and 2002, and at hospital C between 2001 and 2002. Enhanced barriers were not used at any time during the surveillance period at hospital A.

Health care worker compliance with handwashing, CVC site care, and intravenous administration set care was poor at the beginning of the surveillance period.<sup>29,30</sup> Two separate intervention studies, one focused on improving hand hygiene and another focused on improving care of CVC insertion sites and intravenous administration sets, were implemented at the study centers in June 1999 at hospital B and December 2000 at hospital C. Administrative support for similar interventions at hospital A was poor.<sup>29</sup> These interventions significantly reduced the rates of CVC-associated BSI and the results of these studies have been published elsewhere.<sup>29,30</sup>

### Nosocomial infection surveillance and data collection

All patients with a CVC-associated BSI detected by prospective nosocomial surveillance who were admitted to the study ICUs were enrolled and included in the study. An infection control nurse at each study center extracted data prospectively from patient charts. The principal investigator (V. D. R.) trained the data collectors at each center before initiation of the study.

The patient's age, sex, hospital name, type of ICU, average severity of illness score (ASIS), length of stay (LOS), and antibiotic use in the form of defined daily dose (DDD) were recorded on each study patient. Study center data collection sheets were checked for potential errors and missing items by the study coordinator (V. D. R.) to confirm each diagnosis of CVC-associated BSI.

Active surveillance for CVC-associated BSIs was performed at each study center beginning in 1998 and ending in 2002; surveillance was performed from July 1998 to August 2000 in hospital A, from April 1999 to June 2002 in hospital B, and from September 2000 to June 2002 in hospital C. The BSI rate decreased with education and performance feedback in hospital B after June 1999, and in hospital C after December 2000.<sup>30</sup>

### Definitions

CVC-associated BSIs were defined using the Centers for Disease Control and Prevention definitions as follows.<sup>31</sup>

"Laboratory-confirmed BSI" was defined using 2 criteria. Criterion 1 was that the patient had a recognized pathogen cultured from 1 or more percutaneous blood cultures and the pathogen cultured from the blood was not related to an infection at another site. When common skin commensals (eg, diphtheroids, *Bacillus*, *Propionibacterium*, coagulase-negative staphylococci, or micrococci) were recovered, the organism must have been cultured from 2 or more blood cultures drawn on separate occasions. Criterion 2 was that the patient had at least 1 of the following signs or symptoms: fever ( $>38^{\circ}\text{C}$ ); chills; or hypotension, which were not considered to be related to an infection at another site.

"Clinical primary nosocomial sepsis" was defined as the patient having at least 1 of the following clinical signs, with no other recognized cause: fever ( $>38^{\circ}\text{C}$ ) or hypotension (systolic pressure  $<90$  mm Hg); or oliguria ( $<20$  mL/h), but blood cultures were not obtained or no organisms were recovered from blood cultures and there was no apparent infection at another site and the physician instituted treatment for sepsis.

### Culture techniques

Decisions to take catheter samples and obtain blood cultures were made independently by the patient's attending physicians. Specimens not immediately cultured were refrigerated at  $4^{\circ}\text{C}$ . All cultures were inoculated within 8 hours of catheter removal. Standard laboratory methods were used to identify microorganisms in blood and catheter samples.<sup>32</sup>

### Case and control selection and matching

Patients with CVC-associated BSI and control patients without CVC-associated BSI who were hospi-

talized for 7 days or more were matched for the hospital to which they were admitted, ICU type, year they were admitted to the study ICU, LOS, sex, age, and ASIS.<sup>35</sup> Each case patient was matched to 1 control patient.<sup>34</sup>

### Cost estimation

The patient's LOS in the ICU was obtained prospectively on daily rounds. Each hospital's finance department provided the fixed cost per bed-day. The pharmacy provided the DDD<sup>55</sup> of antibiotic use for patients in each ICU and their associated costs. A list of direct costs for each study patient was obtained from each study center's finance department, which calculated the actual cost-to-charge ratio for each patient or their average daily cost. Before January 2002, the Argentinean peso to American dollar exchange rate was 1:1 and all costs in all patients were generated on this conversion ratio. An ongoing economic crisis in our country resulted in a marked devaluation of the Argentinean peso after January 2002. Only 2 of 122 case patients were included in this time period, and no changes were expected to have altered significantly the results of the entire study. Extra cost attributable to BSI was defined as the estimated median difference in direct costs between a patient who was infected and his or her matched patient who was uninfected. The LOS and the direct costs were compared.

### Outcomes

The primary outcomes evaluated in this study included additional days of hospitalization, extra cost, and attributable mortality of CVC-associated BSI.

### Statistical methods

Software (EpiInfo, Version 6.04b, CDC, Atlanta, Ga) was used for data analysis. Baseline differences between treatment groups were analyzed using chi-square analyses for dichotomous variables and Student *t* test for continuous variables. When appropriate, Fisher exact probability test was used. Relative risk ratios, 95% confidence intervals, and *P* values were determined for all primary and secondary outcomes.

### RESULTS

During the study period (July 1998-June 2002), 7284 adult patients were admitted to the study ICUs and a CVC-associated BSI developed in 213 (2.92%). Of those, 142 (66.6%) had a LOS  $\geq$  7 days and were included in the study. A total of 142 control patients, matched for LOS  $\geq$  7 days, hospital location, type of ICU, sex, age, and ASIS were paired with case patients. Incomplete matching on the basis of year of hospitalization occurred in 20 patients (14%), otherwise

**Table 1.** Baseline characteristics of patients

	Case patients (N = 142)	Control patients (N = 142)
Average length of stay $\geq$ 7d (%)	142 (100)	142 (100)
Mean age (SD)	70.09 ( $\pm$ 14.17)	68.88 ( $\pm$ 13.74)*
No. males (%)	83 (58.5)	83 (58.5)*
No. admitted to medical/surgical ICU (%)	116 (81.7)	116 (81.7)*
Mean ASIS (SD)	3.30 ( $\pm$ 1.08)	3.09 ( $\pm$ 0.90)*
Number included in study by year (%)		
1998	25 (17.6)	27 (19.0)
1999	50 (35.2)	49 (34.5)
2000	46 (32.4)	37 (26.1)
2001	19 (13.4)	27 (19.0)
2002	2 (1.4)	2 (1.4)

ASIS, Average severity of illness score; ICU, intensive care unit.

\*No statistical difference found.

baseline characteristics were not different between case and control patients (Table 1). In instances where an exact match between case and control patients could not be made on the basis of year of hospitalization, a control patient from the immediate preceding or following year was used.

Cumulative number of ICU days in patients was 3322 and 1632 in control patients, resulting in average number of days of hospitalization per patient of 23.39 in patients versus 11.9 days in control patients. The cumulative extra days of hospitalization in case patients was 1690, with a mean excess LOS per case patient of 11.9 days (Table 2).

The cumulative fixed costs of CVC-associated BSI for case patients were \$830,500 and \$408,000 for control patients, resulting in \$422,500 extra fixed costs with a mean fixed extra cost per episode of CVC-associated BSI of \$2,975.35 (Table 2).

After adjusting for the added costs of antibiotic use in case and control patients, it was found that the cumulative total costs of CVC-associated BSI was \$1,131,988 for patients with CVC-associated BSIs and \$437,832 for patients without CVC-associated BSIs. This resulted in an additional \$694,156 of total costs with a mean fixed excess cost per episode of CVC-associated BSI of \$4888.42 (Table 2).

Case patients were significantly more likely to have received antimicrobial therapy, with a mean 22.6 extra antibiotic DDD (Table 2).

Of the case patients, 77 (54.2%) died, and 42 (29.6%) of the control patients died, for an attributable mortality of CVC-associated BSI of 24.6% (Table 2).

### DISCUSSION

The most important risk factor for BSI is CVC.<sup>4,10-12</sup> Patients who are critically ill often require prolonged CVC and have a high risk for the development

**Table 2.** Extra expenditures and mortality of central venous catheter-associated bloodstream infections

	Case patients (N = 142)	Control patients (N = 142)	Attributable extra expenditures
Cost of hospitalization			
Total days	3322	1632	1690
Average length of stay in ICU	23.39 (SE 1.49)	11.49 (SE 0.68)	11.9
Total fixed cost	\$830,500	\$408,000	\$422,500
Mean fixed cost	\$5848 (SE 372.89)	\$2873 (SE 171.07)	\$2975
Antibiotic use			
Total antibiotics (in DDD)	4568	1356	3212
Mean antibiotic use per patient (in DDD)	32.16 (SE 2.81)	9.54 (SE 1.05)	22.62
Total cost of antibiotics	\$301,488	\$29,832	\$271,656
Mean costs of antibiotics per patient	\$2123 (SE 186.06)	\$210 (SE 23.09)	\$1913
Total costs			
Aggregate costs	\$1,131,988	\$437,832	\$694,156
Mean aggregate costs per patient	\$7971.74 (SE 537.22)	\$3083.32 (SE 184.53)	\$4888.42
Average mortality	77/142 (54.2%)	42/142 (29.6%)	24.6%

DDD, Defined daily doses; ICU, intensive care unit.

of BSI.<sup>36,37</sup> When CVC-associated BSI does occur, a majority of studies have found an increased attributable mortality ranging from 4% to 37%<sup>2,5,9,38,39</sup> although this association has not been a universal finding.<sup>7,40</sup>

In contrast, almost all studies that have sought to evaluate the impact of CVC-associated BSI on patient outcomes have found significantly increased health care costs and excess LOS in patients in whom this type of nosocomial infection developed. For example, Pittet et al<sup>5</sup> investigated the incremental cost of CVC-associated BSI, using a matched case-control design and found an excess cost per infection of \$29,000 and 14 extra ICU days. Similarly, a matched case-control study published by Digiovine et al<sup>7</sup> found that CVC-associated BSIs were associated with an excess cost of \$34,508 and mean excess LOS of 10 days. Finally, Orsi et al<sup>13</sup> found a mean additional LOS of 19.1 days and 16,356 Euros of extra costs in patients in the ICU in whom a CVC-associated BSI developed.

We found that CVC-associated BSI was associated with an average excess cost of \$4888 and an extra LOS of 11.9 days per episode. The excess health care costs found in our study are significantly less than those reported in recent studies,<sup>5,7,13</sup> however, it must be pointed out that Arnow et al<sup>41</sup> found that the cost of CVC-associated BSI was only \$3707 per episode in 1991. Our study may underestimate the true cost of CVC-associated BSI in other countries that routinely use expensive medical technologies not readily available in Argentina. For example, the average cost per day of hospitalization in most US centers is more than 4 to 5 times greater than in Argentina. As a result, our fixed costs per day of hospitalization are significantly lower than that seen in other hospitals from more developed parts of the world even after correcting for

the value of the dollar. Notwithstanding, we were able to show that CVC-associated BSIs significantly increased the costs of caring for these patients.

Increased antibiotic use is a common finding in studies of nosocomial infection. Our study was no different as we found a mean 23 additional antibiotic DDD in patients with CVC-associated BSI, which accounted for \$1913 of the mean excess health care costs per episode. The excess use of antibiotics has important implications for patients in the ICU setting where the risk of acquiring resistant nosocomial pathogens may be further amplified.<sup>42</sup> Thus, prevention of CVC-associated BSIs may not only reduce health care costs through reducing LOS and antibiotic use, but may also reduce the antibiotic pressure that is driving the selection of resistant micro-organisms in hospitals.<sup>43</sup>

Finally, our findings are concordant with other studies that have found an increased mortality with CVC-associated BSI.<sup>2,5,9,38,39</sup> It is possible that the nearly 25% attributable mortality seen in this and other trials is an artifact of the measurement techniques used (ie, ASIS or other severity of illness scores calculated at ICU admission rather than at the moment of onset of CVC-associated BSI).<sup>40</sup> One limitation of our study was the inability to measure severity of illness scores on a daily basis in our study hospitals. Future studies must seek to use more rigorous analytic methods, such as time series analysis,<sup>44</sup> to evaluate the true impact of CVC-associated BSI on mortality. However, until more data are available the preponderance of current evidence suggests that CVC-associated BSIs are associated with excess patient mortality and our data are consonant with this body of evidence.

Multifaceted programs to prevent CVC-associated BSI that emphasize the application of interventions shown to be useful, such as rigorous handwashing,

vascular catheter care, and judicious antimicrobial use, are needed in hospitals in Argentina. Our data suggest that successful implementation of such programs would significantly reduce patient mortality while at the same time resulting in considerable cost savings and reduced length of hospitalization.

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