

ORIGINAL ARTICLE

Healthcare-Associated Bloodstream Infections Secondary to a Urinary Focus: The Québec Provincial Surveillance Results

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OBJECTIVE. Urinary tract infections (UTIs) are an important source of secondary healthcare-associated bloodstream infections (BSIs), where a potential for prevention exists. This study describes the epidemiology of BSIs secondary to a urinary source (U-BSIs) in the province of Québec and predictors of mortality.

DESIGN. Dynamic cohort of 9,377,830 patient-days followed through a provincial voluntary surveillance program targeting all episodes of healthcare-associated BSIs occurring in acute care hospitals.

SETTING. Sixty-one hospitals in Québec, followed between April 1, 2007, and March 31, 2010.

PARTICIPANTS. Patients admitted to participating hospitals for 48 hours or longer.

METHODS. Descriptive statistics were used to summarize characteristics of U-BSIs and microorganisms involved. Wilcoxon and χ^2 tests were used to compare U-BSI episodes with other BSIs. Negative binomial regression was used to identify hospital characteristics associated with higher rates. We explored determinants of mortality using logistic regression.

RESULTS. Of the 7,217 reported BSIs, 1,510 were U-BSIs (21%), with an annual rate of 1.4 U-BSIs per 10,000 patient-days. A urinary device was used in 71% of U-BSI episodes. Identified institutional risk factors were average length of stay, teaching status, and hospital size. Increasing hospital size was influential only in nonteaching hospitals. Age, nonhematogenous neoplasia, *Staphylococcus aureus*, and Foley catheters were associated with mortality at 30 days.

CONCLUSION. U-BSI characteristics suggest that urinary catheters may remain in patients for ease of care or because practitioners forget to remove them. Ongoing surveillance will enable hospitals to monitor trends in U-BSIs and impacts of process surveillance that will be implemented shortly.

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In the province of Québec, Canada, healthcare-associated bloodstream infections (BSIs) are monitored through the Surveillance Provinciale des Infections Nosocomiales (SPIN; Provincial Nosocomial Infection Surveillance programs). The first program monitors central line-associated bloodstream infections (CLABSIs) in intensive care units (ICUs) and is mandatory for ICUs with 10 beds or more.¹ The second program monitors hemodialysis-related BSIs.² The third program monitors methicillin-resistant *Staphylococcus aureus* (MRSA), including community-associated MRSA.³ The fourth program (Bactériémies-surveillance totale [BACTOT]) is voluntary and began on April 1, 2007, and it collects data on all healthcare-associated BSIs. BACTOT annual reports showed that BSIs secondary to a urinary source (U-BSIs) were the second most common cause of BSIs (first in nonteaching hospitals), after CLABSIs, and present the highest potential

for prevention.^{4,5} Although surveillance results on urinary tract infections (UTIs) and on BSIs are available, detailed information on the epidemiology of U-BSIs is scarce.⁶⁻¹⁰ Consequently, the objectives of this study were to describe the epidemiology of U-BSIs in Québec and explore determinants of mortality associated with U-BSI cases.

METHODS

Data Source

BSIs reported in BACTOT from April 1, 2007, to March 31, 2010, were included in the analysis. This voluntary program targets all acute care hospitals with 1,000 or more admissions per year. Variables available in the BACTOT database are demographic characteristics of BSI cases (gender, date of birth, and birth weight) and characteristics of the episodes

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(date of episode, origin, associated devices or procedures, type of healthcare unit, time from admission to BSI, underlying medical conditions, complications, microorganisms involved with their antimicrobial susceptibility profiles). Patient-days are stratified by hospital and ICU for each administrative period (13 four-week periods per year, beginning on April 1). Participating hospitals were required to report data for at least 6 administrative periods per year. BACTOT is a passive surveillance program that relies on healthcare practitioners to determine the BSI origin. Tools are available for participating professionals, and training is offered periodically to assist them in the adjudication of cases. A coordinating nurse and an infectious diseases specialist with expertise in surveillance are available to assist with complex cases. Only obviously misclassified BSIs and incorrect values (eg, dates) are validated.

Definitions

The definition used for BSIs in the SPIN is described in detail elsewhere¹ and is based on the National Healthcare Safety Network (NHSN) definitions.¹¹ To be considered as healthcare associated, a BSI cannot be present nor incubating at the time of admission (within 48 hours from admission), except if it resulted from a preceding admission or procedure.¹¹ A BSI is considered secondary to a urinary focus when the practitioner determines that a UTI (positive culture) preceded the BSI. The UTI is considered associated with a procedure or urinary device if in place or removed within 7 days of the infection. The 7-day criterion was applied at the time of data collection and was based on the NHSN's definition of asymptomatic bacteriuria.^{11,12} This criterion probably leads to a higher proportion of U-BSIs associated with a urinary device, compared with the NHSN definition, although most devices are likely still in place upon onset of the UTI leading to BSI.

Analysis

U-BSIs characteristics were first compared with nonurinary BSIs. Categorical variables were compared using a χ^2 test, and the Wilcoxon test was used for nonnormal distributions. U-BSIs rates were calculated per 10,000 patient-days. U-BSI episodes were distributed according to the unit of acquisition, involved microorganisms, patients' underlying conditions, and potential risk factors and outcomes.

Poisson regression was first used to identify institutional determinants that could explain U-BSI in participating hospitals, but because of overdispersion, negative binomial regression was used. Each hospital's average length of stay (LOS; patient-days per admissions), teaching status, and size (number of beds) were included in the models. The linearity of rates and of log-transformed rates through continuous and categorized values of LOS and hospital size were assessed to see whether categories of these variables should be used. The

final model was chosen using the Akaike information criterion.¹³

Logistic regression was used to determine which individual determinants were associated with all-cause mortality at 30 days in U-BSI patients. Available potential determinants were age, gender, involved microorganisms, LOS before BSI onset, use of a urinary catheter or of another device, presence of underlying risk factors (diabetes, hematogenous and non-hematogenous neoplasia, neutropenia, total parenteral nutrition, dialysis, bone marrow or solid organ transplant), as well as characteristics of admitting hospitals (average LOS, teaching status, and size). U-BSIs episodes for which survival at 30 days was not specified were excluded from the first model, as well as episodes with incomplete information on tested determinants. Sensitivity analyses were conducted where all episodes with missing information on survival were treated either as being still alive (most probable) or as being dead (least probable). Only variables with $P < .2$ in bivariate analyses were kept for the multivariate analyses, but the final models were chosen based on the Akaike criterion. Analyses were done using SAS 9.2.

RESULTS

Description of All BSIs and U-BSIs

During the 2007–2010 surveillance years, 61 of 89 eligible acute care hospitals (69%) participated in the BACTOT program (20 of 26 teaching hospitals and 41 of 63 nonteaching hospitals). Nonparticipating hospitals were smaller, with the majority nonteaching, and had a higher proportion of older patients. The shortest participation was 13 of 39 periods. Forty-three hospitals had complete participation. Participating hospitals followed 9,377,830 patient-days and reported 7,217 episodes, in 6,959 individual patients, for a rate of 6.6 BSIs per 10,000 patient-days (95% confidence interval [CI], 6.4–6.7). Primary BSIs represented nearly half of all BSIs (48%). CLABSI were the most frequent etiology (28%); U-BSIs came second, with 21% of all BSIs (1.4 U-BSIs per 10,000 patient-days; 95% CI, 1.3–1.5). Although patients with U-BSIs were older than patients with other types of BSIs, U-BSI episodes tended to occur in less critical conditions: U-BSIs were less frequently acquired in ICUs, and their 30-day, all-cause mortality was lower compared with other types of BSIs (Table 1). However, U-BSI episodes still occurred relatively more frequently in ICUs compared with general or other specialized wards, with a rate of 1.8 U-BSIs per 10,000 patient-days (ICU) versus 1.4 U-BSIs per 10,000 patient-days (other inpatient wards; $P = .02$). Males had a higher occurrence of U-BSIs (61%) as well as other BSIs (59%). Only 25 U-BSI episodes were identified in patients younger than 18 years of age, mainly in those younger than 2 years of age.

Microbiology

Five percent of episodes were polymicrobial. Of the 1,594 microorganisms isolated during the 1,510 U-BSI episodes,

TABLE 1. Comparison of Bloodstream Infections (BSIs) Secondary to a Urinary Focus (U-BSIs) with All Other Episodes of BSIs

	U-BSIs (n = 1,510)		Other BSIs (n = 5,707)	
	n	%	n	%
Unit ^a				
ICU	113	7	1,099	19
General or other specialized units	1,213	80	3,713	65
Outpatient	184	12	895	17
Gender				
Female	595	39	2,361	41
Male	915	61	3,346	59
All-cause mortality at 30 days ^{a,b}	194	15	1,097	22
Age, mean, years (median) ^c	70.3 (74)	...	60.0 (64)	...
LOS before BSI, mean, days (median) ^c	28.8 (13.5)	...	31.2 (15)	...

NOTE. ICU, intensive care unit; LOS, length of stay.

^a Significant difference between U-BSIs and other BSIs (χ^2 test).

^b Percentages were calculated using only episodes for which the survival status was known (87% of episodes).

^c Significant difference between U-BSIs and other BSIs (Wilcoxon test).

almost half were *Escherichia coli* (47%). Other Enterobacteriaceae (including *Klebsiella* sp.) represented one-fifth (22%) of all isolates (Figure 1). One hundred twenty (8%) were *S. aureus*, with 37 isolates being MRSA (31% of all *S. aureus*). Of 737 *E. coli* strains tested for susceptibility to ciprofloxacin, 123 (17%) were resistant; 85 (17%) of tested strains of *E. coli*, *Klebsiella* sp., and *Proteus* sp. were extended-spectrum β -lactamase producers. Three of 29 *Candida* sp. were resistant to fluconazole (10%). Three of 96 (3%) *Enterococcus faecium* or *faecalis* were resistant to vancomycin.

Risk Factors

Among individual risk factors for UTIs, use of urinary devices remained the most prevalent and was reported in 71% of all episodes (60% had a urinary catheter). Diabetes (30%) and the presence of a nonhematogenous neoplasia (22%) were the most frequent underlying medical conditions in patients with U-BSI. Forty-six percent (583/1,269) of the episodes for which the information was complete for all collected underlying conditions occurred in patients without any underlying conditions, 39% in patients with 1 condition, and 15% in patients with at least 2 conditions.

Analyses to identify hospital-level risk factors (or characteristics associated with increased rates) initially included data from 61 hospitals. A small teaching hospital with an abnormally high average LOS (31 days) was excluded. In bivariate analyses, an increase of 1 day in the average LOS of patients in a hospital was found to be associated with an increase of 10% of hospitals' U-BSI rates; an increase of 50 beds was also associated with an increase of 13% in rates; nonteaching hospitals presented rates almost 2 times lower than teaching hospitals (Table 2). On the basis of the Akaike information criterion, the multivariable model with the best data fit in-

cluded the 3 available variables (average LOS, teaching status, and number of beds), as well as an interaction term between hospital size and teaching status. Table 2 details rate ratios accounting for this interaction. An increase of 1 day in the average LOS was thus associated with an increase of 7% in U-BSI rates. Larger hospital sizes were associated with higher rates but only in nonteaching hospitals, and as hospital size increased, teaching and nonteaching rates became more and more similar.

Complications

A readmission was reported for at least 6% (79/1,326) of U-BSIs acquired in previously hospitalized patients. Twelve percent (149/1,274) of all episodes required a transfer to the ICU, and in 15% (194/1,278 episodes), patients died (all cause) within 30 days of the episode's onset. In deceased patients, *E. coli* was the microorganism most frequently isolated (42% of isolated microorganisms; 86 of 206), followed by *Klebsiella* sp. (13%; n = 26), *S. aureus* (11%; n = 22), and *Pseudomonas aeruginosa* (9%; n = 17). Eleven percent (7/62) of tested strains of *E. coli*, *Klebsiella* sp., and *Proteus* sp. produced extended-spectrum β -lactamase, and 27% (6/22) of *S. aureus* strains were MRSA. When restricting the analysis to episodes with complete information, the all-cause mortality at 30 days was 15% (194/1,278). We estimated that U-BSI all-cause mortality was at least 13% (194/1,510) if missing information on survival at 30 days was interpreted as still being alive at the end of the follow-up period, and it could increase to 28% (426/1,510) if missing information on survival was treated as being dead.

In the logistic regression model comparing the relative frequency of characteristics in patients who died and in those who survived when all information was complete, 7 char-

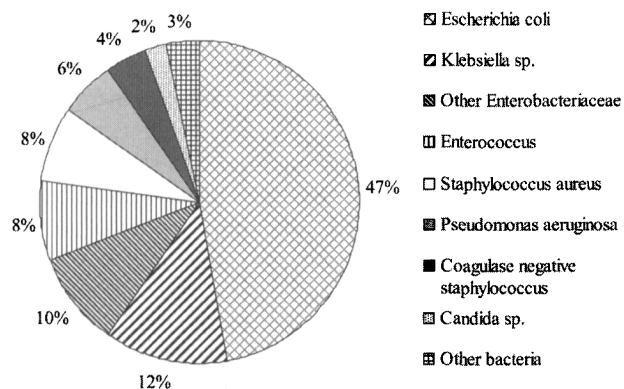


FIGURE 1. Distribution of microorganisms involved in reported bloodstream infections secondary to a urinary focus ($n = 1,594$).

acteristics were kept for multivariable analysis since they were associated with death, using a bivariate cutoff P value of 0.20 (Table 3; all available characteristics are listed in "Methods"). In the final model, increasing age (1.02; 95% CI, 1.00–1.03), the presence of a Foley catheter (vs no device; 1.85; 95% CI, 1.14–3.00), identification of *S. aureus* (2.01; 95% CI, 1.07–3.77), and a preexisting hematogenous (3.00; 95% CI, 1.57–5.75) or nonhematogenous (1.88; 95% CI, 1.22–2.89) neoplasia were the only determinants associated with an increased risk of death, while being in a teaching hospital (0.62; 95% CI, 0.42–0.94) seemed protective. Preexisting diabetes, although not statistically significant, helped lower the Akaike information criterion. The 2 sensitivity analysis models allowed the inclusion of 124 additional episodes. Age, non-hematogenous neoplasia, urinary devices, and the presence of *S. aureus* in blood cultures were the 4 variables included

in all 3 models. Episodes excluded from the main model because of missing values tended to be older, were less frequently in teaching hospitals, reported Foley catheters use more frequently, reported less preexisting neoplasia, and were more likely to be bacteremic with *E. coli*.

DISCUSSION

The BACTOT surveillance program was in its first 3 years of data collection in 2007–2010, but the network already had a vast healthcare-associated BSI surveillance experience with its MRSA and CLABSIs mandatory surveillance programs. Among the available variables, there was only 1 determinant that infection control and prevention teams could modify: use of urinary devices. This exploration of the SPIN data on U-BSIs has shown that this well-known UTI risk factor is frequently reported in U-BSI episodes, and its use is associated with increased mortality. Although data on the cause of death are too incomplete and subjective, forcing us to study instead all-cause mortality, it is still obvious that U-BSIs are less frequently associated with death compared with other healthcare-associated BSIs, even though they occur in older patients. These results are of interest because of the large number of cases followed and detailed.

Our global BSI rate (6.6 BSIs per 10,000 patient-days; 95% CI, 6.4–6.7) was slightly higher than the rate observed in France in 2004 (6.1 BSIs per 10,000 patient-days; 95% CI, 5.9–6.3), with a similar proportion of U-BSIs (21%) of which, similar to our data, half were caused by *E. coli*.⁷ However, French participating hospitals could be different from ours, and our ability to compare both rates further is limited. In the European Antimicrobial Resistance Surveillance System, 20% of isolated *E. coli* were resistant to fluoroquinolones,

TABLE 2. Hospital Characteristics Associated with Rates of Bloodstream Infections Secondary to a Urinary Focus (U-BSIs)

	Hospitals ($n = 60$)	Rates per 10,000 patient-days (95% CI)	Rate ratios (95% CI)	
			Bivariate	Multivariate ^a
LOS, mean, days	60	1.41 (1.33–1.49)	1.10 (1.03–1.18)	1.07 (1.02–1.13)
Hospital size ^b	60	1.41 (1.33–1.49)	1.13 (1.08–1.18)	
In teaching hospitals				1.02 (0.99–1.04)
In nonteaching hospitals				1.23 (1.20–1.26)
Academic status				
Teaching	19	1.69 (1.58–1.80)	1.0	1.0
Nonteaching	41	1.01 (0.98–1.17)	0.56 (0.43–0.73)	
If 100 beds				0.50 (0.25–0.99)
If 150 beds				0.56 (0.31–1.20)
If 200 beds				0.74 (0.37–1.46)
If 250 beds				0.89 (0.45–1.77)

NOTE. CI, confidence interval; LOS, length of stay.

^a Multivariate results account for the interaction between hospital size and the academic status and show (1) the rate ratio per 50 additional beds according to the academic status of the hospital and (2) the expected rate ratio for teaching status as the number of beds increases (hypothetical hospital sizes are shown since the number of beds is a continuous variable).

^b Per additional 50 beds.

TABLE 3. Determinants of Mortality in Episodes of Bloodstream Infections Secondary to a Urinary Focus (U-BSIs) at 30 Days after the Infection Onset

	U-BSI (n)	Deaths (n) ^a	Bivariate OR ^a	Multivariate OR (95% CI)	P
Age	861	129	1.02	1.02 (1.00–1.03)	.016
Academic status					
Nonteaching	305	54	1.0	1.0	
Teaching	556	75	0.73	0.62 (0.42–0.94)	.022
Hematogenous neoplasia					
No	796	113	1.0	1.0	
Yes	65	16	1.97	3.00 (1.57–5.75)	.001
Nonhematogenous neoplasia					
No	661	89	1.0	1.0	
Yes	200	40	1.61	1.88 (1.22–2.89)	.004
Diabetes					
No	611	83	1.0	1.0	
Yes	250	46	1.44	1.39 (0.92–2.09)	.114
Urinary devices					
None	229	29	1.0	1.0	
Foley catheter only	374	75	1.73	1.85 (1.14–3.00)	.014
Other device only	160	16	0.77	0.75 (0.38–1.48)	.411
Foley and other device	98	9	0.70	0.57 (0.25–1.29)	.175
<i>Staphylococcus aureus</i>					
No	793	113	1.0	1.0	
Yes	68	16	1.85	2.01 (1.07–3.77)	.030
<i>Pseudomonas</i> sp.					
No	815	119	1.0	...	
Yes	46	10	1.63

NOTE. CI, confidence interval; OR, odds ratio.

^a Only the determinants with $P < .2$ in bivariate analyses are shown.

while 17% of our isolates were resistant to ciprofloxacin.¹⁴ Our proportion of *S. aureus* resistant to methicillin (31%) is comparable with the proportion found by the provincial MRSA program (32%) in 2008.³ Even though women are known to be at greater risk for uncomplicated UTIs, only 39% of our U-BSIs occurred in women, which is consistent with results from a smaller study.¹⁵ U-BSIs do not develop frequently in patients with UTIs, but the large numbers of healthcare-associated UTIs inevitably lead to an important number of U-BSIs.^{9,10,16} A nonnegligible proportion of patients with catheter-related asymptomatic bacteriuria will develop a U-BSI (1%–4%).⁹ Our results seem consistent with the known epidemiology of U-BSIs.

Three institutional risk factors for the development of U-BSI were explored in our regression analyses. In Québec, teaching hospitals tend to be larger and deal with a more complex patient population who might require longer LOS. As suspected, hospital rates were influenced by all 3 available variables, but the main result of the negative binomial regression model is the evidence of an interaction between hospital size and teaching status: larger hospitals and teaching hospitals of any size tended to be similar, while smaller nonteaching hospitals had lower rates. In other publications, BSI rates are often presented according to hospital size and teaching status, and individual LOS (especially while catheterized)

is a known risk factor for UTIs.^{4,6,7,9,16–18} There might therefore be room for improvement of hospitals' U-BSI rates by reducing rates of UTIs through a decrease use of catheterization and its duration, but this cannot be analyzed since the proportion of catheterized non-U-BSI patients is not available.^{16,19,20} Although the prevalence of diabetes and neoplasia in U-BSI patients was higher in our study when compared with the entire Québec population (prevalence of 5.9% for diabetes and cumulative incidence of 1% on a 5-year basis for neoplasia),^{21,22} we cannot assume that these conditions are risk factors for U-BSIs without obtaining the equivalent information for all non-U-BSI patients in our participating hospitals.

Although U-BSI patients were older than patients with BSIs from other sources, they seemed to die less during their BSI episode. Half of our U-BSIs were caused by *E. coli*, while bacteria associated with a higher risk of death at 30 days, such as *S. aureus*, were much less frequent. Age, diabetes, and neoplasia were also determinants of mortality, but they could also have been direct causes of mortality rather than simple underlying conditions. We hypothesize that nonteaching hospitals have patients with less severe underlying medical conditions that could decrease their risk of BSI. However, once a patient is sick, care is likely more aggressive in teaching hospitals, which could explain the decreased mortality.

Our study has some limitations, such as voluntary participation in the surveillance program. It is interesting to note that more than two-thirds of all eligible hospitals participated on their own initiative, but little is known about those that did not enter the program. Because these hospitals tend to have fewer beds and to be nonteaching, in accordance with our regression results, we suspect that their entry in the program would lower the global U-BSI rates. Our regression models were limited by the availability of variables, especially in the case of the negative binomial modeling of U-BSI rates. In this model, only institutional variables were available, since individual-level information on patients without U-BSI was unavailable. This implies that we studied hospitals rather than patients themselves, which reduced the variety of observations (only 60 hospitals). Use of Foley catheters and resistance to antimicrobials are among the information that would have been of interest to compare with non-U-BSI cases. Finally, and unfortunately, the causal relationship between death and U-BSI (related or not) was missing for half of the deceased cases and was shown not to be standardized across hospitals, since it is left to the hospital epidemiologists and preventionists to adjudicate (R. Gilca et al., unpublished data, 2007). Only 861 of the 1,510 episodes (57%) could be included in the main model and 985 (65%) in the sensitivity analyses, because of missing data on the available determinants. More advanced imputation techniques could possibly help, although the subjectivity underlying the process would still be a concern.

Our U-BSI rates are influenced by hospitals teaching status, size, and average LOS. A majority of cases had a urinary catheter in the week before BSI onset. In our data, academic status of the hospital, age, neoplasia, urinary devices, and some microorganisms were significant determinants of U-BSI mortality. Patients that developed U-BSIs were often in teaching hospitals and were non-ICU patients, with few comorbidities. This suggests that urinary catheters may be kept in more chronic patients on the wards for ease of care or because practitioners forget to remove them. Targeted prevention strategies should be prioritized. Because participation in surveillance programs has apparently helped hospitals reduce their CLABSI rates, we are hoping that the efforts invested in the surveillance of all healthcare-associated BSIs and, more specifically, of U-BSIs will lead to the same trend in the years to come.²³ Finally, the implementation of process surveillance to monitor the compliance with catheter insertion technique and timely removal should lead to improved U-BSI rates. Ongoing surveillance is thus crucial.

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