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The Impact of Nosocomial Bloodstream Infections on Mortality, Length of Stay and Hospital Costs in Older Adults

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Abstract

Background—Nosocomial bloodstream infections (BSI) are hazardous and costly events. This study was undertaken to quantify the impact of nosocomial BSI on older patients, including mortality, length of stay (LOS), and costs attributed to BSI.

Methods—A multi-state, multi-center, matched, retrospective cohort study was conducted from January 1994 through June 2002 in eight hospitals from the Southern-Central United States. Patients aged > 65 years with nosocomial BSI were enrolled. Controls without bloodstream infection were matched to cases. Outcomes during the 90-day period following hospital discharge were evaluated to determine the association between BSI and mortality, hospital costs, and LOS.

Results—Eight-hundred thirty cases and 830 matched controls were identified, all with a mean age of 74.4 years. Among cases, 81% of BSIs were central line-associated and *Staphylococcus aureus* was the most common pathogen accounting for 34.6% of infections (2/3 were methicillin resistant). The mortality rate of cases was 49.4%, compared to 33.2% for controls (OR 2.1, $p < 0.001$), LOS was 29.2 days for cases and 20.2 days for controls ($p < 0.001$), and hospital charges

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were \$102,276 for cases compared to \$69,690 for controls ($p < 0.001$). The mean LOS and mean costs attributable to BSI were 10 days and \$43,208, respectively.

Conclusion—Nosocomial BSI in older adults was significantly associated with increases in 90-day mortality, increased LOS, and increased costs of care. Preventive interventions to eliminate nosocomial BSIs in older adults would likely be cost effective.

Keywords

BSI; Hospital-acquired; MRSA; Elderly; Bacteremia; outcome

Blood-stream infections (BSIs) are common nosocomial infections and have been one of leading causes of death in US hospitals since 1999.¹ The estimated number of nosocomial BSIs in US hospitals was 215,000 in 2002,² with an incidence of 2.2 cases per 100 admissions (with a range of 0.6 cases/100 admissions among all hospitalized patients and 9.7 cases/100 admissions in intensive care units).^{3–5} The impact of BSIs has been well described in the general population, with reported mortality attributable to nosocomial BSI ranging from 21% to 69%; attributable costs ranging from \$23,000 to \$56,000; and excess length of stay (LOS) ranging from 2 to 32 days.^{3, 5–14} Of note, these estimates were derived from general patient populations with scant data focusing on older patients.

The elderly population in the US is rapidly increasing and is expected to increase from 40 million in 2010, to more than 80 million by 2050.¹⁵ As far as we know, no studies have focused exclusively on the impact of BSI in older adults, which is surprising because BSI rates increase with age, from 4.47 per 1,000 patients among those aged 65–74 to 18.1 per 1,000 patients among those aged >85 years.^{16, 17} The impact of BSI on older adults is of particular relevance, since the majority of older adults in the US have healthcare coverage provided by the Centers for Medicare and Medicaid Services (CMS). CMS has been basing payments to hospitals in part on rates of central line-associated BSI (CLABSI), and had been holding reimbursements related to CLABSI acquired in hospitals since October of 2008.¹⁸ Thus, given the likely continued increase over time in the frequency of BSI in older adults and increasing regulation and reimbursement tied to the incidence of BSI, it is important to better understand the epidemiology and outcomes associated with BSI in older adults.¹⁹ The aims of this study were to determine the impact of BSI on clinical outcomes of older adults, including mortality, length of hospital stay (LOS), and hospital costs.

Methods

Study Design and Study Population

This was a retrospective cohort study conducted in 8 hospitals, including one 750-bed tertiary care university hospital and 7 community hospitals, in North Carolina and Virginia that were members of the Duke Infection Control Outreach Network (DICON). Institutional review boards (IRBs) at all participating centers had approved the study before its initiation.

All patients were 65 years or older. Cases were defined as those patients who had 1 positive blood culture after 48 hours of hospitalization between 01/01/1994 and 06/01/2002 and met criteria for BSI per CDC definitions.²⁰ All centers used standard CDC surveillance

criteria and methods.²⁰ Controls were matched to cases in a 1:1 ratio. Matching parameters included: 1) hospital, 2) unit, 3) calendar year, and 4) time at risk (i.e. time from admission to culture for patients with BSI). For controls, the total duration of hospital stay had to be at least as long as the time at risk of their matched case. Controls were selected randomly by applying an automatic random number-generating function to the list of eligible patients.

Epidemiologic Variables

Patient and microbiologic information were prospectively entered into a database including culture date, hospital location, pathogen name, resistance phenotypic profile, presence of central-venous catheter (CVC), and anatomic site of CVC insertion. A uniform epidemiologic data collecting tool was constructed prior to study initiation, and additional data that were retrospectively collected included gender, race, age, admission source, insurance type, the presence of various comorbid conditions, the Charlson co-morbidity score,²¹ McCabe Score,²² presence of indwelling medical devices at the time of hospital admission, body mass index (BMI), ICU stay prior to culture date for cases and during the hospitalization for controls, and surgeries prior to culture date for cases and during the hospitalization for controls. Obesity was defined as BMI > 30. Functional status was measured as independent or not independent for 5 activities of daily living (ADLs,) defined by Katz et al.²³ A binary variable for functional status was created as well to measure severe disability which was defined as lack of independence with ≥ 3 ADLs. A binary variable was also created for the Charlson score,²¹ using a breakpoint of ≥ 3 . Primary (i.e. central line-associated) BSI and secondary (non central line-associated) BSI were defined according to standard CDC criteria and definitions.²⁴ Outcomes measured for the 90 days following bloodstream infection (including hospital re-admissions) for cases and admission date for controls included length of stay, hospital charges and mortality. Hospital charge data were obtained from hospital financial databases.

Statistical Analysis

All analyses were performed by using SAS software (9.2, Cary, NC). The t-test and Wilcoxon Rank Sum test were used to analyze continuous variables and the Chi-square and Fisher's exact were used for bivariate analyses. For the multivariate model building, variables with a P value of < 0.20 in the bivariate analyses were included as candidate variables. Final models included variables with an adjusted P value ≤ 0.05 . All p values were two-sided. Logistic regression was used to identify independent predictors of 90-day mortality. Linear regression (after log transformation) was used to develop risk models for LOS and hospital charges. Patients with missing charge data were excluded from the hospital charges analysis. Inverse log value was calculated for beta coefficients of variables included in the models for LOS and hospital charge. Attributable outcomes per BSI were calculated as the mean difference between a BSI patients and uninfected controls with the following formula: attributable outcomes per BSI = ([mean outcomes for uninfected] \times [inverse log of beta coefficient for adjusted BSI variable]) - (mean outcomes for uninfected).

Results

Eight hundred and thirty cases with BSI were identified and 830 uninfected matched control patients were selected. The mean age of all patients was 74.4 years; 50.8% were male and 69.9% were Caucasians. There were 416 cases (50.1 %) and 422 controls (51.3%) who had a Charlson score greater than 2. Severely impaired functional status at admission (lack of independence with ≥ 3 ADLs) was reported in 426 (52%) cases and 460 (56%) controls.

Among cases, 672 (81%) BSIs were categorized as primary (e.g. central line-associated). The mean and median durations of hospital stay before BSI occurred were 12 and 9 days, respectively. The most common BSI pathogen was methicillin-resistant *Staphylococcus aureus* (MRSA) (23%), followed by methicillin-susceptible *S. aureus* (MSSA) (10.6%), *Enterococcus* species (6.1%), and coagulase-negative staphylococci (5.4%). Two hundred-forty BSIs (28.9%) were caused by Gram-negative pathogens. Table I displays the bivariate analysis of cases versus controls, in terms of background conditions, co-morbid conditions, and outcomes. Per bivariate analysis, compared to controls, cases were more frequently obese, more often had recent surgery, had increased severity of acute illness indices, and more frequently had a central line or gastrostomy tube at the time of hospital admission.

Mortality

In bivariate analysis (Table II), cases were significantly more likely to die than were controls (410/830 [49%] of cases died vs. 276/830 [33%] mortality rate among controls, $p < 0.001$). In multivariate analysis (Table III), BSI was a significant independent predictor for 90-day mortality with an odds ratio (OR) of 2.08 (95%-CI 1.69~2.57). Other independent predictors for mortality were lack of independent functional status at the time of hospital admission, elevated Charlson co-morbidity score,²¹ presence of a rapidly fatal condition at the time of admission,²² presence of an immunosuppressing condition, malignancy with metastases, and age > 75 years. Chronic connective tissue disease and hemiplegia were associated with decreased risk for mortality (Table III).

Duration of hospitalization

In bivariate analyses (Table II), the median LOS for cases and controls were 23.0 [IQR: 14–36] and 15.0 [IQR: 8–27] days ($p < 0.0001$) and the mean LOS was 29.2+27.5 and 20.2+18.0 days ($p < 0.0001$).

In multivariate analysis, BSI was associated with a 1.5 fold increase in duration of hospitalization (95% CI: 1.42~1.65), after adjusting for age, Charlson score, liver disease, dialysis, metastatic malignant disease and the presence of a rapidly fatal underlying condition.²² The mean LOS attributable to an episode of BSI was 10 days (95% CI: 8.4~13.0).

Hospital charges

Hospital charges were available for 622 cases and 597 controls. In bivariate analysis (Table II), cases had a significantly higher medians and means of hospital charges compared to controls (i.e. median of \$65,037 [IQR=33,097–120,395] and mean of \$102,276±118,790 for

cases vs. median of \$35,596 [IQR=15,774–82,883] and mean of \$69,690±88,430 for controls, $p<0.001$ for both comparisons). Subjects with missing data were compared to those without missing data. No significant differences between these two groups were identified with regards to age, gender or type of insurance.

In multivariate analysis, BSI was associated with 1.63 fold increase in hospital charges after adjusting for marital status, obesity, Charlson score,²¹ myocardial infarction, dementia, hemodialysis, metastatic malignant disease and functional status (95% CI: 1.44~1.84). The mean hospital charges attributable to an episode of BSI were \$43,208 (95% CI: 30,663~58,540).

Discussion

This study demonstrates the significance and magnitude of adverse outcomes associated with BSI among hospitalized older adults. Among older adults, an episode of BSI was associated with a greater than 2 fold increased mortality, 10 extra days of hospitalization and greater than \$43,000 of additional hospital charges. Eighty-one percent of the BSIs were CLABSI which was higher than the rates reported among the general population (56%–66%).^{14, 25} The relatively high proportion of CLABSI among older adults might be related to increased severity of acute illness, increased frequency of invasive procedures and higher prevalence of comorbid conditions for which patients might require a central line in order to be adequately treated.²⁶

Since many CLABSI are preventable,¹ by investing resources in preventing CLABSI in older adults, there is potential to prevent many deaths and save hospitals significant costs. Costs associated with BSI are particularly important, since CMS is basing reimbursement to hospitals in part, on rates of CLABSI. The cost figures in this study do not reflect the potential impact of CMS. Thus cost-savings opportunities related to CLABSI prevention are even greater than this study suggests. Initiatives to focus on CLABSI prevention should focus on catheter insertion, maintenance and prompt removal.

The most common BSI pathogen was *S. aureus* (33%) and two third of *S. aureus* isolates were MRSA. This is similar to previous studies of BSI in older adults as well as in the general population.^{25, 27} BSI due to *S. aureus* in older adults is associated with a 2-fold increase in mortality, which is very similar to findings in the current study.^{26, 28} The predominance of MRSA as a BSI pathogen in older adults is of particular concern because MRSA is associated with particularly poor outcomes.

The study has limitations. Its retrospective cohort design with matched groups, subject it to some sampling bias. The fact that enrollment was terminated over a decade ago might affect the results of the study because of advances in prevention and treatment of CLABSI and changes in location of treatment such as IV therapy at home. Although the age of the data does not affect the internal validity of the study, the magnitude of the impact of BSI on study outcomes could possibly be different between data collected in 1994–2002 and data collected more recently. Major strengths of this study are its multicenter nature, the large sample size, and the strict matching parameters applied to the selection of controls. The fact

that controls were as chronically sick and functionally dependent as cases, suggests that they were a true representation of the source population from which cases arose, and further strengthen the reported independent significant associations between BSI and poor outcomes among elderly and explains in part why these results differed from prior studies.^{27, 28}

BSIs have a devastating impact on older adults. The study findings provide even greater rationale in older adults for strengthening the considerable efforts that experts have made in preventing IV catheter-related infections, such as focusing on catheter insertion, maintenance and prompt catheter removal. In addition, more rapid and accurate methods of diagnosing BSI and CLABSI would improve the timeliness of appropriate clinical patient management, including catheter removal and implementation of effective antimicrobial therapy. Older adults are among the most vulnerable hospitalized populations and one of the most rapidly growing patient populations. Optimizing care of older adults with regards to BSI prevention and management represents a major challenge to healthcare providers and administrators, but also a great opportunity to improve healthcare for older adults.

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Table I

Baseline characteristics and bivariate analysis of cases and controls

Baseline character	Cases (n=830)	Controls (n=830)	OR (95%CI)
Demographics			
Age, median (interquartile)	74.08 (69–78)	74.67 (69–79)	NA
Age >75 years	315 (38.0)	327 (39.4)	0.94 (0.77–1.15)
Male sex (%)	445 (53.6)	399 (48.5)	1.23 (1.01–1.50)
Married Marital status (%)	493 (59.8)	456 (55.5)	0.84 (0.69–1.03)
Medicare health insurance (%)	835 (97.3)	808 (98.1)	1.02 (0.71–1.45)
Admit not from home (%)	340 (41.3)	306 (37.2)	1.20 (0.98–1.49)
Co-morbid scores and conditions			
Charlson's score, mean	3+2.3	3+2.2	NA
>2 Charlson's co-morbidities (%)	416 (50.1)	422 (51.3)	0.95 (0.77–1.15)
Rapidly fatal McCabe score at admission (%)	195 (23.6)	159 (19.3)	1.39 (1.06–1.82)
Body mass index, mean	26.6±6.0	25.5±6.0	NA
Obese, body mass index > 30 (%)	179 (22.9)	137 (17.8)	1.39 (1.08–1.80)
Congestive heart failure (%)	177 (21.3)	168 (20.4)	1.07 (0.83–1.37)
Connective tissue disease (%)	32 (3.9)	36 (4.4)	0.82 (0.50–1.36)
Chronic obstructive pulmonary disease (%)	150(18.1)	165 (20.0)	0.88 (0.69–1.13)
Cerebral vascular attack (%)	129 (15.5)	106 (12.9)	1.25 (0.94–1.65)
Dementia (%)	73 (8.8)	56 (6.8)	1.36 (0.94–1.98)
Diabetes (%)	222 (26.8)	193 (23.4)	1.20 (0.96–1.51)
Myocardial infarction (%)	166 (20.0)	182 (22.1)	0.87 (0.68–1.11)
Peptic ulcer disease (%)	96 (11.6)	96 (11.7)	1.00 (0.74–1.36)
Diabetes with end organ damage (%)	38(4.6)	38 (4.6)	1.00 (0.63–1.58)
Dialysis (%)	48 (5.8)	38 (4.6)	1.35 (0.83–2.18)
Hemiplegia (%)	14 (1.7)	17 (2.1)	0.82 (0.41–1.67)
Human immunodeficiency virus infection (%)	1 (0.12)	0	NA
Immunosuppressant usage (%)	99 (12.0)	94 (11.5)	1.03 (0.75–1.40)
Metastatic malignancy (%)	75 (9.0)	93 (11.3)	0.71 (0.49–1.04)
Functional status (Activities of daily living, i.e. ADL)			
Dependent on Bathing (%)	452 (54.5)	504 (60.8)	0.75 (0.61–0.93)
Dressing (%)	439 (52.9)	456 (55.4)	0.90 (0.73–1.10)
Feeding (%)	281 (33.9)	326 (39.7)	0.75 (0.61–0.93)
Ambulation (%)	478 (57.6)	520 (63.2)	0.77 (0.62–0.95)
Urine incontinence (%)	266 (32.2)	232 (28.2)	1.26 (1.00–1.58)
Bowel incontinence (%)	152 (18.3)	121 (14.7)	1.37 (1.04–1.81)
ADL assistance 3 at admission (%)	426 (51.95)	460 (56.0)	0.84 (0.68–1.03)
Exposures to nosocomial environments, procedures, and devices			

Baseline character	Cases (n=830)	Controls (n=830)	OR (95%CI)
Foley at admission (%)	118 (14.2)	119 (14.3)	0.99 (0.74–1.32)
Gastrostomy at admission (%)	30 (3.6)	15 (1.8)	2.25 (1.14–4.44)
Central line at admission (%)	128 (15.4)	73 (8.8)	1.85 (1.37–2.50)
ICU stays prior to culture (%)	317 (38.3)	NA	NA
Intubation prior to culture (%)	214 (25.9)	NA	NA
Vasopressors use prior to culture (%)	117 (14.2)	NA	NA
Surgery prior to culture in current hospitalization (%)	317 (38.8)	282 (34.4)	1.33 (1.03–1.73)
Outcomes			
Mortality (%)	49	33	<0.01
Length of hospital stay, median (interquartile)	23 (14–36)	15 (8–27)	<0.01
Hospital charges, median (interquartile)	\$65037 (33097–120395)	\$35596 (15774–82883)	<0.01

NA: not available.

¹ Defined as taking steroid or other immunosuppressant medications on admission.

Table II

Bivariate analysis of 90-day Mortality

Baseline Character	Dead in 90 days, n=686	Alive in 90 days, n=974	OR (95% CI)
BSI	410 (59.8)	420 (43.1)	1.96 (1.61–.39)
Demographics			
Age (>75)	284 (41.4)	358 (36.8)	1.22 (1.00–1.49)
Sex (male)	372 (54.2)	472 (48.8)	1.26 (1.04–1.53)
Marital (married)	277 (40.7)	421 (43.6)	0.89 (0.73–1.09)
Insurance (CMS)	11 (1.6)	24 (2.5)	0.65 (0.31–1.33)
Co-morbid scores and conditions			
Obese	119 (18.8)	197 (21.5)	0.83 (0.64–1.07)
Charlson score (>2)	411 (60)	427 (44.2)	1.87 (1.53–2.28)
Congestive heart failure	167 (24.3)	178 (18.4)	1.44 (1.13–1.83)
Connective tissue disease	23 (3.4)	45 (4.7)	0.71 (0.43–1.19)
Chronic obstructive pulmonary disease	153 (22.3)	162 (16.8)	1.44 (1.12–1.84)
Cerebrovascular accident	106 (15.5)	129 (13.3)	1.19 (0.90–1.57)
Dementia	60 (8.8)	69 (7.1)	1.24 (0.87–1.79)
Diabetes	178 (26.0)	237 (24.5)	1.08 (0.86–1.35)
Myocardial infarction	143 (20.9)	205 (21.2)	0.98 (0.77–1.25)
Peptic ulcer diseases	84 (12.2)	108 (11.2)	1.11 (0.82–1.50)
Dementia	30 (4.4)	46 (4.8)	0.92 (0.58–1.48)
Dialysis	41 (6.0)	45 (4.7)	1.31 (0.85–2.02)
Hemiplegia	8 (1.2)	23 (2.4)	0.49 (0.22–1.10)
HIV	1 (0.15)	0	--
Immunosuppressant ¹	109 (15.9)	84 (8.7)	2.00 (1.48–2.71)
Malignancy metastasis	103 (15.0)	65 (6.7)	2.47 (1.78–3.43)
McCabe (rapid fatal)	177 (25.8)	177 (18.4)	1.57 (1.24–1.98)
Functional status (Activities of daily living, e.g. ADL)			
ADL baseline (>2)	191 (28.7)	185 (19.4)	1.64 (1.30–2.06)
Dependent on bathing	212 (31.8)	210 (21.9)	1.63 (1.30–2.03)
Dependent on dressing	197 (29.5)	194 (20.3)	1.62 (1.23–2.03)
Dependent on feeding	107 (16.0)	101 (10.5)	1.60 (1.19–2.14)
Dependent on ambulation	245 (36.7)	289 (30.1)	1.32 (1.07–1.62)
Urine incontinence	87 (13.1)	88 (9.22)	1.26 (1.07–2.00)
Bowel incontinence	72 (10.8)	72 (7.5)	1.47 (1.04–2.07)
Exposures to nosocomial environments, procedures, and devices			
Foley at admission	125 (18.2)	112 (11.5)	1.72 (1.30–2.26)
Gastrostomy at admission	21 (3.1)	24 (2.5)	1.25 (0.69–2.26)
ICU stay ²	172 (42.2)	145 (34.5)	1.38 (1.04–1.83)

Baseline Character	Dead in 90 days, n=686	Alive in 90 days, n=974	OR (95% CI)
Intubation ²	128 (31.4)	86 (20.5)	1.78 (1.29–2.43)
Vasopressor ²	86 (21.2)	31 (7.4)	3.37 (2.18–5.22)
Surgery ²	217 (31.9)	382 (39.9)	0.72 (0.58–0.88)

¹ Defined as taking steroid or other immunosuppressant medications on admission.

² Prior to surgery in current admission for cases and during current hospitalization for control. Percentage in parenthesis.

Table IIIIndependent predictors of 90-day mortality ($p < 0.05$)

Predictors	Dead (n=686)	Alive (n=974)	OR	95% CI
BSI ^A	410 (59.8%)	420 (43.1%)	2.08	1.69–2.57
Age >75 years	284 (41.4%)	358 (36.8%)	1.26	1.02–1.56
Charlson score ≥ 3	191 (28.7%)	185 (19.4%)	1.76	1.41–2.20
Immunosuppressive state ^B	109 (15.9%)	84 (8.7%)	2.00	1.44–2.77
Metastatic Malignancy	103 (15%)	65 (6.7%)	2.21	1.53–3.19
Rapidly fatal state per McCabe score	177 (25.8%)	177 (18.4%)	1.50	1.16–1.95
Deteriorated functional status ^C	191 (28.7%)	185 (19.4%)	1.65	1.33–2.06
Connective tissue disease	23 (3.4%)	45 (4.7%)	0.56	0.32–0.97
Hemiplegia	8 (1.2%)	23 (2.4%)	0.32	0.14–0.74

^A Bloodstream infection^B Immunosuppressant used on admission.^C Dependent in ≥ 3 activities of daily living (ADL) per Katz criteria