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Major Article

Risk of subsequent health care–associated infection among patients with a bloodstream infection present on hospital admission

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Background: The risks and outcomes of acquiring a health care–associated infection (HAI) among patients with a bloodstream infection present on hospital admission (BSI-POA) have not been well described. The objective of this study was to examine the incidence of and risk factors for developing a subsequent HAI and to compare length of stay and mortality between patients with a BSI-POA who develop an HAI and those who do not.

Methods: This was a retrospective cohort study of patients aged ≥18 years discharged with a BSI-POA from 3 hospitals in New York City between 2006 and 2014.

Results: There were 761 HAIs among the 11,436 patients with a BSI-POA. Incidence rates were: catheter-associated urinary tract infections, 5.03 infections per 1,000 catheter days; pneumonia, 2.7% among BSI-POA patients; surgical site infections, 9.2% among BSI-POA patients. Length of stay was longer among patients who developed an HAI (mean ± SD, 35.0 ± 29.8 vs 12.4 ± 11.9, $P < .001$). Mortality was higher in patients who developed an HAI (23.9% vs 11.6%, $P < .001$).

Conclusions: Risk factors for those who developed an HAI differed by infection type. Overall, HAI was associated with longer hospitalization, and pneumonia was associated with increased mortality.

Health care–associated infections (HAIs) are among the most common complications of hospital care, with over 700,000 events occurring annually and affecting 1 in 25 hospitalized patients.[1] Nearly 99,000 deaths occur each year from HAIs, making this the 10th leading cause of death, with a projected annual cost of $9.8 billion. The burden of disease attributable to HAIs is a major patient safety issue and has resulted in regulatory action, such as financial penalty, from the Centers for Medicare and Medicaid Services.[1,2]

All hospitalized patients are at risk of developing HAIs, but the risk may be greater in individuals already medically compromised, such as those with a bloodstream infection present on hospital admission (BSI-POA), among whom factors such as organ dysfunction, multiple comorbidities, and increased use of invasive devices are common.[3] A subsequent HAI may cause greater severity of illness, longer hospital stay, and higher risk of mortality.[4] Conditions associated with immune compromise, such as diabetes mellitus,[5] malignancies,[6] HIV, and renal failure,[7,8] predispose patients to opportunistic infections. However, associations between these exposures and HAI among individuals with a BSI-POA have not been specifically examined. Identifying contributing factors could potentially reduce health care expenditures, length of stay, and mortality.[9] Hence, the aims of this study were to examine the incidence of and risk factors for developing a subsequent HAI among patients with a BSI-POA and compare length of stay and mortality between patients with a BSI-POA who develop HAI and those who do not.

METHODS

Design, setting, and sample

This retrospective cohort study used data obtained from a large electronic database that merged clinical and administrative data from all inpatient admissions from a large academic health system located in New York City for the years 2006-2014. Data collected included over 700,000 discharges of patients ≥18 years of age from a 300-bed community hospital and 2 tertiary and quaternary care hospitals

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with 650 and 850 beds, respectively. The sample for this study is a subset of the entire study population and included 11,436 patients ≥18 years of age with a BSI-POA. Institutional review board approval was obtained with a waiver of individual consent.

Data collection

Data extracted included (1) demographics; (2) laboratory reports; (3) device utilization data, such as urinary catheter and mechanical ventilation; (4) patient medical history; (5) inpatient record, including previous hospitalization, length of stay, and intensive care unit (ICU) stay; (6) skilled nursing facility (SNF) stay; (7) Charlson Comorbidity Index (CCI);[10] and (8) ICD-9-CM codes for the following conditions: renal failure, malignancies, HIV, and diabetes mellitus. The HAIs examined included catheter-associated urinary tract infection (CAUTI), pneumonia, and surgical site infection (SSI).

Study definitions

Patients who presented with a BSI ≤48 hours of admission and had no history of hospitalization within the previous 30 days were considered to have a BSI-POA. BSI-POA was defined as a positive blood culture with any organism of interest identified ≤48 hours of admission. Definitions of HAI were modified using concurrent surveillance definitions from the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) (www.cdc.gov/nhsn/about.html). HAIs (CAUTI, pneumonia, and SSI) were defined as occurring >48 hours after hospital admission and were based on electronically available criteria. In cases where specific data were not available electronically (eg, urinary symptoms), a team of clinicians and researchers developed algorithms to identify infections as described in Apte et al.[11] In previous work, central line duration and dates of diagnosis were 100% consistent between the electronic algorithms and expert chart review.[12] CAUTIs were defined as occurring between 1 day after urinary catheter insertion and 72 hours after removal, with positive urine culture with any organism, that is, $\geq 10^5$ colony-forming units (CFU) per mL of urine and no more than 1 other species of microorganism or positive urine culture with any organism, that is, 10^3-10^5 CFU/mL of urine and no more than 1 other species of microorganism and pyuria (≥3 white blood cells per high-power field on urine microscopy) within ± 48 hours of positive culture. The diagnosis of pneumonia was based on ICD-9-CM coding for pneumonia, including all pneumonia codes and positive respiratory cultures with any organism.[11] SSI was defined as any performed NHSN operative procedure (ICD-9-CM procedure code) and positive wound culture for any organism within 30 days following the procedure.[13]

Statistical analysis

The incidence of each HAI was calculated by dividing the number of infections by the total population at risk during the study period. For CAUTI, this was the number of urinary tract infections per 1,000 catheter days; for pneumonia, the number of pneumonias per total patients with BSI-POA; for SSI, the number of SSIs per number of patients with BSI-POA undergoing a surgical procedure. Descriptive statistics were computed, including percentages and frequency tables for categorical variables and mean, median, and SD for continuous variables. The relationships between each type of infection and potential predictors or confounding variables were calculated. For categorical variables, χ^2 tests were used, and continuous variables were calculated using the Student *t* test for age and Wilcoxon signed-rank test for CCI. Odds ratios (ORs) and 95% confidence intervals (CIs) were computed for all associations, and statistical significance was determined using a *P* value of <.05. Multicollinearity tests were performed, and variables with highly correlated predictors were removed from each model. Multiple logistic regression models were then created for each outcome variable (CAUTI, pneumonia, and SSI). The variables examined as potential confounders were sex, age, renal failure, malignancy, HIV, diabetes mellitus, ICU stay, previous stay in a SNF, and CCI.[10,14] HIV was not included in the multivariate analysis for SSI because of the small sample size. For patients with more than 1 admission during the data collection period, only the first admission was included.

Multiple logistic regression models were used to examine length of stay among patients who developed HAIs versus those who did not for 2 categories, each based on median length of stay: 3-10 days (reference category) and 11-60 days. We truncated length of stay from 3-60 days because a <3-day stay did not meet HAI criteria and a >60-day stay resulted in a few outliers that would markedly distort the analysis.[15] For SSI, we categorized surgical procedures that occurred in the operating room as ≥30 minutes in duration (long procedures) or <30 minutes (short procedures). Because many patients who died had a short length of stay, we removed them from the length of stay analysis.

Finally, multiple logistic regression models—using the same covariates as those examined for length of stay—were used to determine if patients who developed HAIs were at increased risk of death compared with patients who did not develop HAIs. Data analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Characteristics of the study population

The study included 11,436 patients with a BSI-POA. The mean age for the population was 64.41 years (SD ± 18.27). Male patients accounted for 53.9% of the population. Clinical comorbid conditions included renal failure (38.2%), diabetes mellitus (30%), malignancy (21.3%), and HIV (5.6%). A total of 7.3% of patients were transferred from an SNF, and 28.1% had an ICU stay during their hospitalization.

Among the 11,436 patients with a BSI-POA, 761 (6.7%) developed an HAI (CAUTI, pneumonia, or SSI). CAUTI incidence rate was 5.03 infections per 1,000 catheter days. There were 306 (2.7%) pneumonia cases, 69% of which occurred among patients on mechanical ventilation. Among patients with a BSI-POA who had a surgical procedure, a total of 170 of 1,852 (9.2%) developed an SSI.

Risk factors for HAI

Table 1 compares the incidence and risk factors for infection by infection type. ICU stay and CCI were significant risk factors for CAUTI. ORs (95% CI) were 2.25 (1.75-2.89) and 1.04 (1.01-1.09), respectively. Significant risk factors for pneumonia were male sex (1.35, 1.06-1.71), malignancy (1.48, 1.08-2.04), HIV (2.17, 1.18-4.02), and ICU stay (10.50, 7.90-13.95). Significant risk factors for SSI were diabetes mellitus (1.79, 1.19-2.69), ICU stay (1.95, 1.29-2.93), and CCI (1.03, 1.01-1.12).

HAI and length of stay

The median length of hospital stay for all patients with a BSI-POA was 9 days for those without an HAI compared with 29, 31, and 25 days for those who developed a CAUTI, pneumonia, or SSI, respectively ($P < .001$) (Fig 1). In the multivariate analysis, after controlling for sex, ICU stay, age, CCI, and duration of surgery in the SSI model, length of stay was significantly higher in patients with the 3 types of HAIs compared with those without HAIs. Age was not a significant predictor of length of stay for any of the 3 types of infections, but the

Table 1
Multivariate analysis for variables associated with specific type of health care–associated infection among patients admitted with a bloodstream infection

Variables	CAUTI: N = 285		Pneumonia: N = 306		SSI: N = 170	
	N (%)	OR (95% CI)	N (%)	OR (95% CI)	N (%)	OR (95% CI)
Male (ref = female)	139 (48.7)	0.83 (0.65-1.05)	205 (67)	**1.35 (1.06-1.71)**	66 (38.8)	1.40 (0.91-3.83)
Renal failure	132 (46.3)	0.91 (070-1.18)	152 (49.7	1.07 (0.83-1.37)	77 (45.3)	1.01 (0.67-1.50)
Malignancy	54 (18.9)	0.76 (0.52-1.10)	83 (27.1)	**1.48 (1.08-2.04)**	14 (8.2)	0.54 (0.27-1.04)
HIV	14 (4.9)	1.26 (0.60-2.65)	23 (7.5)	**2.17 (1.18-4.02)**	3 (1.8)	†
Diabetes mellitus	85 (29.8)	0.96 (0.72-1.27)	79 (25.8)	0.91 (0.68-1.21)	72 (42.4)	**1.79 (1.19-2.69)**
ICU stay	180 (63.2)	**2.25 (1.75-2.89)**	243 (79.4)	**10.50 (7.90-13.95)**	98 (57.7)	**1.95 (1.29-2.93)**
SNF stay	26 (9.1)	0.85 (0.56-1.29)	32 (10.5)	**1.46 (1.02-2.16)**	11 (6.47)	1.45 (0.67-3.13)
Age*: mean [SD]	66.3 [17.7]	0.99 (0.99-1.00)	63.8 [16.9]	0.99 (0.92-1.01)	60.4 [13.60]	0.99 (0.98-1.00)
CCI*: mean [SD]	3.05 [2.64]	**1.04 (1.01-1.09)**	3.21 [2.56]	0.93 (0.90-1.01)	2.71 [2.25]	**1.03 (1.01-1.12)**

Note. Bold values are statistically significant ($P < .05$).
CAUTI, catheter-associated urinary tract infection; *CCI*, Charlson Comorbidity Index; *CI*, confidence interval; *ICU*, intensive care unit; *OR*, odds ratio; *ref*, reference; *SD*, standard deviation; *SNF*, skilled nursing facility; *SSI*, surgical site infection.
*Continuous variable.
†n = 3 (too small).

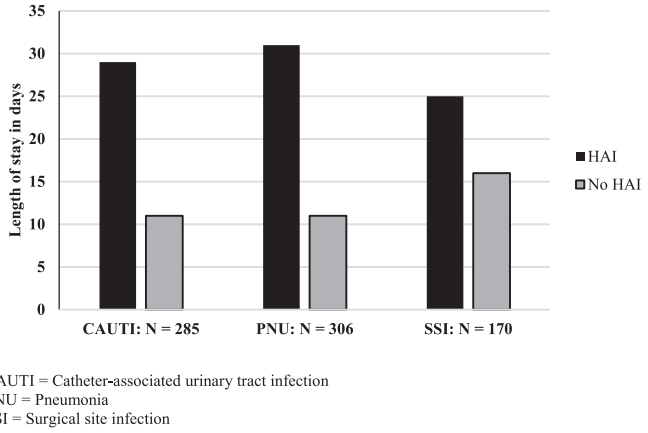

Fig 1. Median length of stay among patients admitted with a bloodstream infection with and without an HAI. Univariate analysis using Wilcoxon signed-rank test to compare length of stay in the HAI versus the non-HAI group. *P* values <.001 for all comparisons. *CAUTI*, catheter-associated urinary tract infection; *HAI*, health care–associated infection; *SSI*, surgical site infection.

odds of a longer stay were significantly greater for each type of infection among those with ICU stays and higher CCI scores (Table 2).

HAI and mortality

The mortality rate for patients who developed an HAI was 23.9% compared with 11.6% for those who did not develop an HAI ($P < .001$). Three models were specified—1 for each type of infection—to describe the associations between HAIs and mortality after adjusting for sex, ICU stay, age, CCI, and surgery duration in the SSI model. There was no significant relationship between having a CAUTI or SSI and mortality, but those who had pneumonia were more likely to die (OR, 1.87, 95% CI, 1.43-2.44). Across all types of HAI, ICU stay, age, and CCI were associated with a significantly higher risk of mortality, and male patients had significantly lower odds of death compared with female patients (Table 3).

DISCUSSION

Types of infections

The overall rate of HAIs in this population was 6.7%. Pneumonia was the most common infection, followed by CAUTI and then SSI. Results from a multistate prevalence survey of HAIs among all hospitalized patients estimated that 157,000 cases of pneumonia occurred in US hospitals in 2011, 39% of which were ventilator-associated[9] compared with 69% observed in our study. Another study examined ICU patients in Greece and reported that ventilator-associated pneumonia accounted for 56.1% of all HAIs.[16] Differences may be attributable to variations in geographic location, hospital or surveillance practices, or the possibility that patients admitted with a BSI are at greater risk of this more serious infection.

The rate of CAUTI in this study (5.03 per 1,000 catheter days) was slightly higher than that reported in national data from NHSN acute care hospitals (1.2-4.8 per 1,000 catheter days)[17] and in another study of ICU patients (4.2 per 1,000 catheter days),[16] perhaps reflecting the high-risk nature of patients with a BSI-POA and the use of a definition that was less stringent than that used by NHSN (10^3 as opposed to 10^5 CFU/mL).

A systematic review examined 57 studies published between 2002 and 2012 and reported a median SSI incidence of 3.7%.[18] Another study assessed the burden of HAI in community hospitals and reported an SSI prevalence rate between 0.6 and 4.3%,[19] whereas data from NHSN reported overall SSI rates of 1.9% from 2006-2008.[20]

Table 2
Length of stay by type of infection among patients admitted with a bloodstream infection

Variables	Length of stay		
	CAUTI: N = 285 OR (95% CI)	Pneumonia: N = 306 OR (95% CI)	SSI: N = 170 OR (95% CI)
Infection	5.88 (4.47-7.72)	7.95 (5.85-10.81)	1.51 (1.03-2.21)
Surgery: duration ≥ 30 min (ref = < 30 min)	-	-	1.17 (0.93-1.48)
Male (ref = female)	1.09 (0.69-1.23)	1.07 (0.97-1.18)	0.95 (0.77-1.17)
ICU stay	4.89 (4.42-5.42)	4.79 (4.32-5.31)	5.82 (4.77-7.08)
Age*	1.00 (0.99-1.00)	1.00 (0.99-1.00)	0.99 (0.98-1.00)
CCI*	1.09 (1.07-1.11)	1.09 (1.07-1.11)	1.19 (1.14-1.24)

CAUTI, catheter-associated urinary tract infection; *CCI*, Charlson Comorbidity Index; *CI*, confidence interval; *ICU*, intensive care unit; *OR*, odds ratio; *ref*, reference; *SSI*, surgical site infection.
*Continuous variable.

Table 3
Mortality by type of infection among patients admitted with a bloodstream infection

Variables	Mortality		
	CAUTI: N = 285 OR (95% CI)	Pneumonia: N = 306 OR (95% CI)	SSI: N = 170 OR (95% CI)
Infection	0.79 (0.56-1.01)	1.87 (1.43-2.44)	1.14 (0.71-1.83)
Surgery: duration ≥ 30 min (ref = < 30 min)	-	-	0.93 (0.63-1.36)
Male (ref = female)	0.86 (0.76-0.97)	0.85 (0.75-0.97)	0.88 (0.77-0.99)
ICU stay	9.16 (8.05-10.42)	8.69 (7.63-9.89)	9.89 (8.67-11.28)
Age*	1.03 (1.03-1.04)	1.03 (1.02-1.04)	1.03 (1.02-1.04)
CCI*	1.16 (1.13-1.18)	1.15 (1.12-1.18)	1.19 (1.12-1.17)

CAUTI, catheter-associated urinary tract infection; *CCI*, Charlson Comorbidity Index; *CI*, confidence interval; *ICU*, intensive care unit; *OR*, odds ratio; *ref*, reference; *SSI*, surgical site infection.
*Continuous variable.

By contrast, 9.2% of our patient population undergoing surgery developed an SSI, possibly related to differences in populations or data collection methods or, again, a higher risk of subsequent infection in patients admitted with a BSI. Hence, for the 3 types of HAI examined, rates in our BSI-POA population were slightly higher than those reported in the literature for hospitalized patients in general.

Risk factors for HAI

Not surprisingly, ICU stay was associated with CAUTI, pneumonia, and SSI after adjusting for sex, renal failure, malignancy, HIV, diabetes, admission from an SNF, age, and CCI. Severely ill patients in the ICU typically require extended hospitalization and increased use of invasive devices and are more vulnerable to developing HAIs.

CCI was originally developed and validated as a risk of mortality score but is often also used as a predictor of other outcomes, such as length of stay and HAI, with less consistent results. One study reported no correlation between CCI scores among patients with and without device-associated HAIs,[16] although another found higher CCI scores in patients who developed HAIs.[21] In 1 recent study, no association was observed between higher CCI scores and SSI,[22] whereas Khan et al[23] reported a significant association between higher CCI scores and SSI. A team of researchers has reported higher CCI scores in patients with ventilator-associated pneumonia.[24] In our study, higher CCI scores were significantly associated with CAUTI and SSI but not pneumonia.

HAI and length of stay and mortality

Consistent with previous studies, patients who developed HAIs had significantly longer hospital stays.[25-27] Further, an ICU stay and higher CCI scores were predictive of prolonged length of stay in other studies.[28,29]

Although 1 study reported a higher mortality rate among catheterized patients in a geriatric hospital with CAUTI compared with noncatheterized patients (19.2% vs 10.5%, $P < .05$), there was no statistically significant difference in mortality between catheterized patients with and without CAUTI (19.2% vs 11.3%, $P = .07$).[30] There was no correlation between having a CAUTI and risk of mortality in our population although these patients were primarily older and at higher risk.

In our BSI-POA cohort, pneumonia, ICU stay, age, and higher CCI scores were significant predictors of higher mortality, and men were significantly less likely to die than women. The fact that, overall, male patients had a lower risk of dying when controlling for comorbidities and other risks warrants additional research. We found patients who developed pneumonia were more likely to die compared with those who did not develop pneumonia. Similarly, in a European multicenter prospective study of 201 ICU patients who developed hospital-associated pneumonia, the overall 30-day mortality rate was almost 30%, and those with ventilator-associated pneumonia were significantly more likely to die.[31] Mortality related to ventilator-associated pneumonia is particularly high[32]; 1 team of researchers examined data from 112 patients with carbapenem-resistant Enterobacteriaceae ventilator-associated pneumonia and reported a 30-day mortality of 57.1%.[33] Researchers found that patients who had a major cancer surgery–associated SSI had increased odds of mortality (OR, 3.78, 95% CI, 3.56-4.02).[34] After controlling for duration of surgery, sex, ICU stay, age, and CCI, we found no relationship between SSI and mortality (OR, 1.14, 95% CI, 0.71-1.83).

In 2 recent studies examining cancer patients, the overall HAI rates were higher than the rates observed in this study (31%[35] and 40.7%[14]), which is not surprising since factors associated with malignancies, such as extensive antibiotic use, prolonged exposure to chemotherapeutic agents, invasive intravenous lines, cancer-related complications, and treatment-associated adverse effects, increase the risk of HAIs.[36,37]

Limitations

To our knowledge, this is the first study to examine the incidence of and risk factors for developing a subsequent HAI as well as assess length of stay and mortality among patients admitted to the hospital with a BSI. However, our study does have several limitations. First, it was retrospective in nature and included only data available from electronic records—data that were not collected for research purposes and therefore did not include information on a number of variables that could be associated with risk of HAI or potential confounders. Blood cultures remain the most important tool for diagnosing BSI-POA[38]; however, the possibility of blood culture contamination might have contributed to higher infection rates in our study. Because we included 10^3-10^5 CFU/mL in the definition of CAUTI, the incidence rate is likely higher than in other reported studies. In addition, some HAIs, particularly pneumonia, are difficult to diagnose. In fact, NHSN overhauled ventilator-associated pneumonia definitions in 2014, using criteria shown to be less subject to inter-rater reliability and more reliably associated with clinical outcomes.[39] Hence, it is possible that some HAIs were missed or misdiagnosed. Our study was also conducted in hospitals in a single metropolitan area, so results might not be generalizable to rural communities. Finally, by examining total length of hospital stay, we did not differentiate between length of stay as a cause or an effect of HAI.

CONCLUSIONS

Despite limitations, our findings have important implications for practice. Because risk of HAI among those with BSI-POA differs by infection type, using a risk assessment process to select suitable therapeutic interventions could possibly contribute to a reduction in infection rates and inappropriate use of antimicrobials. In conclusion, this research adds new information about the incidence and risk of HAI in patients with BSI-POA as well as confirmatory evidence of previously identified risk factors. Overall, patients admitted with a BSI

who developed an HAI had a significantly longer length of stay. Neither CAUTI nor SSI was associated with mortality, but pneumonia was a significant predictor of mortality.

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