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ORIGINAL RESEARCH

Impact of Location of Acquisition of Gram-Positive Bloodstream Infections on Clinical Outcomes Among Patients Admitted to Community Hospitals

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Purpose: We investigated the association between location of acquisition (LOA) of gram-positive (GP) bloodstream infections (BSI) in community hospitals and clinical outcomes.

Methods: We performed a multicenter cohort study of adult inpatients with GP BSI in nine community hospitals from 2003 to 2006. LOA was defined by CDC criteria: 1) community-acquired (CA), 2) healthcare-associated (HCA) such as BSI <48 hours after admission plus hospitalization, surgery, dialysis, invasive device, or residence in a long-term care facility in the prior 12 months, and 3) hospital-acquired (HA) as BSI ≥48 hours after hospital admission.

Results: A total of 750 patients were included. Patients with HCA or HA GP BSI were significantly more likely to require assistance with ≥1 activity of daily living, have higher Charlson scores, and die during the hospitalization. Patients with HCA or HA GP BSI were more likely to have BSI due to a multidrug-resistant GP organism, but less likely to receive appropriate antibiotics within 24 hours of BSI presentation. Those with CA BSI were more likely to have a streptococcal BSI and to be discharged home following hospitalization. HA BSI was a risk factor for requiring a procedure for BSI and receiving inappropriate antibiotics within 24 hours of BSI. Both HA and HCA GP BSI were risk factors for in-hospital mortality.

Conclusion: LOA for patients with GP BSI in community hospitals was significantly associated with differences in clinical outcomes including receiving inappropriate antibiotics and in-hospital mortality. Distinguishing LOA in a patient presenting with suspected GP BSI is a critical assessment that should influence empiric treatment patterns.

Keywords: community hospital, bloodstream infection, bacteremia, *Staphylococcus aureus*

Introduction

Bloodstream infections (BSIs) are both common indications for hospital admission and complications that arise during hospitalization. Gram-positive organisms such as *Staphylococcus aureus*, coagulase-negative *Staphylococcus, Enterococcus*, and *Pneumococcus* are not only readily capable of acquiring antimicrobial resistance but can also disseminate to cause BSI. As the rates of antimicrobial resistance increase, administration of appropriate antibiotics for treatment of BSI is increasingly important. Additionally, hospitalizations for *S. aureus* endocarditis have increased and hospitalizations for invasive methicillin-resistant *S. aureus* (MRSA)

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infections remain frequent, both of which can lead to significant morbidity and mortality.[1–4]

The location of acquisition of BSI is a designation of the context in which a patient develops the BSI that is separated into three categories: community-acquired, healthcare-associated, and hospital-acquired. Previous studies have found significant variations in patient outcomes of BSI based upon location of acquisition.[5–7] In fact, healthcare-associated BSI has been identified as an independent risk factor for receiving inappropriate antibiotic therapy.[8] However, much of the previous work in the epidemiology of BSIs has not differentiated from gram-positive vs gram-negative organisms or presentation in academic vs community hospitals.

Within the US, the majority of healthcare takes place in community hospitals,[9] and the understanding of the epidemiology of infections within this setting is evolving. The primary objective of this study is to determine the association between location of acquisition of gram-positive BSI and clinical outcomes among patients in community hospitals. The secondary objective of this study is to determine if risk factors for gram-positive BSI differ by location of acquisition.

Materials and Methods

The data utilized for this study were part of a larger retrospective cohort study of BSI in adults admitted to nine community hospitals in North Carolina and Virginia from 2003–2006 who were either admitted with gram-positive BSI or developed gram-positive BSI over the course of admission.[10] The nine community hospitals were members of the Duke Infection Control Outreach Network. Trained data abstractors collected patient data by chart review utilizing a standardized data collection tool, data dictionary, and standard operating procedures created prior to data abstraction. This study was approved by the Institutional Review Board (IRB) of Duke University Health System, and participating community hospitals deferred to the Duke IRB (n=5) or reviewed and approved the study via their local IRB (n=4). Written patient consent was waived by all sites.

Gram-positive BSIs were defined using modified Centers for Disease Control and Prevention (CDC) criteria as follows: ≥1 positive blood culture for bacterial pathogens, except for common skin contaminants such as coagulase-negative staphylococci or enterococci, which required ≥2 positive blood cultures within 48 hours.[11] Primary BSI was a BSI not related to an infection at another site, while secondary BSI was a BSI with a documented source such as genitourinary, wound, or lower respiratory tract infections. Multidrug-resistant organisms (MDROs) included methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase negative *Staphylococcus*, and vancomycin-resistant *Enterococcus*. The location of acquisition was designated by CDC criteria: 1) "community-acquired" was defined as a BSI occurring <48 hours after admission without one of the above healthcare risk factors; 2) "community-onset, healthcare-associated" was defined as a BSI occurring <48 hours after admission plus the presence of ≥1 of the following healthcare risk factors: prior hospitalization, surgery, dialysis, or residence in a long-term care facility in the 12 months preceding the BSI, or the presence of an invasive device; and 3) "hospital-onset, healthcare-associated" was defined as a BSI that occurred ≥48 hours after hospital admission.

Outcomes of interest for this study included intensive care unit (ICU) admission, hospital length-of-stay, in-hospital all-cause mortality, discharge status, and receipt of appropriate empiric antimicrobial therapy. Discharge status was designated as the patient going home, to a rehab or nursing facility, leaving against medical advice, or being transferred to a tertiary care hospital. Appropriate antimicrobial therapy was defined as receipt of an antimicrobial agent with in vitro activity against the infecting organism, and the antibiotic and route of administration would provide adequate bioavailability for treatment of BSI. Empiric antimicrobial therapy was defined as therapy given within 24 hours after the onset of BSI.

For the statistical analysis, categorical variables were summarized by proportions and the χ^2 test. Continuous variables were summarized by median, interquartile range (IQR), and Kruskal–Wallis Test. Descriptive statistics were performed for the total cohort and then based on location of acquisition. Logistic regression was used for categorical outcomes with odds ratio (OR), 95% confidence interval (CI), and *P*-value reported. Linear regression was used for continuous outcomes with least square means difference, 95% CI, and *P*-value evaluated. Location of acquisition, and Charlson scores were selected as covariates a priori. We constructed our final model using backwards selection. First, covariates were included if $P<0.1$ in bivariable analyses. Covariates were removed from the model if $P>0.05$ until the final model was constructed.

Results

Seven hundred and fifty patients were included in the analysis (Table 1). One hundred and eighty-five (25%) patients had a community-acquired gram-positive BSI, compared to 431 (57%) patients with healthcare-associated BSI and 134 (18%) patients with hospital-acquired BSI. Methicillin-sensitive *S. aureus* (MSSA) was the most common infecting pathogen within the cohort, accounting for 209 (28%) cases of BSI. Six hundred and nineteen (83%) BSIs were defined as primary BSI. Among 131 secondary BSIs, lower respiratory tract infection was the most common source for the cohort (35%).

Univariate analysis of multiple risk factors for infection showed distinct patterns based on the location of acquisition of gram-positive BSI (Table 1). The median age of the patients was 64 years (IQR=51–77). Patients with community-acquired gram-positive BSI were significantly more likely to be male, have ongoing alcohol and tobacco abuse, and to be discharged home. Patients with healthcare associated gram-positive BSI were more likely to be dependent on activities of daily living (ADLs), including dressing, bathing, feeding, and bowel and urine continence ($P<0.001$), be admitted from a nursing facility ($P<0.001$), have dementia ($P<0.001$), congestive heart failure ($P<0.001$), cerebrovascular disease ($P<0.005$), or be dialysis-dependent ($P<0.001$) than those with community-acquired or hospital-acquired BSI. Patients with hospital acquired gram-positive BSI tended to have worse outcomes than patients with community-acquired or healthcare-associated BSIs, including more frequent ICU admission with intubation and vasopressor requirement within 1 week following BSI, and a significantly higher in-hospital mortality rate (27%, $P<0.001$) (Table 2).

Specific pathogens caused BSI based upon location of acquisition (Table 3). Streptococci were the most common infecting pathogens in patients with community-acquired BSI (50%), while MRSA was with most common infecting pathogen in patients with healthcare-associated BSI (31%). Coagulase-negative *Staphylococcus* was the most common cause of gram-positive BSI in patients with hospital-acquired BSI. Notably, MDROs were common causes of gram-positive BSI in this cohort, constituting 31% of cases; the majority of these cases were due to MRSA (79%). *Enterococcus* was an uncommon cause of infection in this cohort (4%); rates of this infection did not significantly vary based on location of acquisition of BSI. Only four patients had BSI due to vancomycin-resistant *Enterococcus*.

Twenty percent of the cohort were not treated with an appropriate antibiotic at any point during the hospitalization, while 43% of the cohort did not receive appropriate antibiotic therapy within the first 24 hours of BSI. Patients with hospital-acquired BSI were significantly less likely to receive appropriate antibiotics within 24 hours of BSI (Table 4).

Adjusted multivariable modeling revealed distinct risk factors for outcomes based on location of acquisition (with community-acquired BSI used as a reference) (Table 5). Healthcare-associated gram-positive BSI was associated with a reduced risk of ICU admission compared to patients with community-acquired BSI (OR=0.61, 95% CI=0.40–0.91, $P=0.02$). However, patients with healthcare-associated BSI were more likely to undergo a procedure for their BSI (OR=2.18, 95% CI=1.17–4.22, $P=0.02$). Patients with hospital-acquired BSI were more likely to be intubated (OR=1.99, 95% CI=1.08–3.68, $P=0.03$). In comparison to patients with community-acquired BSI, patients with hospital-acquired BSI were significantly less likely to receive appropriate antibiotics for Gram-positive BSI within 24 hours (OR=0.48, 95% CI=0.28–0.82, $P=0.007$). Both healthcare-associated and hospital-acquired BSI were risk factors for all-cause in-hospital mortality (OR=2.10, 95% CI=1.17–3.95, $P=0.02$ and OR=2.54, 95% CI=1.29–5.12, $P=0.008$, respectively). Among patients who survived their hospitalizations with gram-positive BSI, those with healthcare-associated BSI and hospital-acquired BSI were at increased risk for 90-day readmission (OR=2.11, 95% CI=1.39–3.26, $P<0.001$ and OR=1.91, 95% CI=1.13–3.24, $P=0.02$, respectively).

Discussion

The present study elucidates the epidemiology of gram-positive BSIs in community hospitals in the Southeastern US through the following findings: 1) gram-positive BSIs in community hospitals are most commonly healthcare-associated infections due to *S. aureus*; 2) many (43%) patients do not receive appropriate antibiotics within the first 24 hours of BSI presentation; 3) location of acquisition of gram-positive BSI has a significant impact on type of pathogen, severity of infection, and risk of in-hospital mortality and 90-day readmission, and 4) location of acquisition was associated with specific, known risk factors for infection.

An improved understanding of the epidemiology of important infections in community hospitals is critical, as they provide the majority of inpatient healthcare in the US. Prior European studies have compared the epidemiology of

Table 1 Patient Demographics, Co-Morbidities, and Hospitalization Information*

	Total Cohort (N=750, 100%) n (%)	Community-Acquired (N=185, 25%), n (%)	Healthcare-Associated (N=431, 57%), n (%)	Hospital-Acquired (N=134, 18%) n (%)	*P*-value
Patient demographics					
Age					
(median; IQ1, IQ3)	64 (51, 77)	60 (48, 72)	66 (52, 79)	64 (52, 76)	0.84
(range)	(18–101)	(18–95)	(23–101)	(19–93)	
Male Sex	383 (51)	112 (61)	200 (46)	71 (53)	0.005
Race					0.41
White	392 (52)	99 (54)	217 (50)	76 (57)	
Black	342 (46)	82 (44)	204 (49)	56 (48)	
Asian	3 (0.4)	0 (0)	2 (0.4)	1 (0.7)	
Hispanic	3 (0.4)	0 (0)	3 (0.7)	0 (0)	
Native American	3 (0.4)	0 (0)	3 (0.5)	0 (0)	
Other	7 (0.9)	4 (2)	2 (0.5)	1 (0.7)	
Insurance					<0.001
Medicare	493 (66)	96 (52)	315 (73)	82 (62)	
Medicaid	70 (9)	13 (7)	45 (10)	12 (9)	
Private	110 (15)	40 (22)	48 (11)	22 (17)	
Unknown	12 (2)	3 (2)	6 (1)	4 (3)	
None	61 (8)	32 (17)	17 (4)	12 (9)	
BMI					
(median; IQ1, IQ3)	27 (22, 33)	27 (22, 33)	26 (22, 32)	27 (23, 32)	0.51
(range)	(13–79)	(12–71)	(14–79)	(14–64)	
Comorbid conditions at Admission					
Need assistance with:					
Ambulation	403 (54)	65 (35)	255 (59)	83 (62)	<0.001
Bathing	205 (27)	19 (10)	150 (35)	36 (27)	<0.001
Dressing	183 (24)	18 (10)	134 (31)	31 (23)	<0.001
Bowel continence	100 (13)	4 (2)	72 (16)	24 (18)	<0.001
Urine continence	170 (23)	20 (11)	117 (27)	33 (25)	<0.001
Feeding	139 (19)	10 (5)	104 (24)	25 (19)	<0.001
McCabe score at admission					<0.001
1	145 (19)	31 (17)	79 (19)	73 (26)	
2	418 (56)	80 (43)	269 (63)	70 (53)	
3	179 (24)	34 (40)	70 (40)	28 (21)	
On immunosuppressive medication					0.99
Corticosteroid	65 (9)	15 (8)	36 (9)	14 (11)	
Non-corticosteroid	13 (2)	3 (2)	8 (2)	2 (2)	
Both	4 (0.5)	1 (0.5)	2 (0.5)	1 (0.8)	
Comorbidities					
Diabetes	330 (44)	81 (44)	197 (46)	52 (39)	0.33
Myocardial infarction	182 (24)	33 (18)	114 (26)	35 (26)	0.06
Congestive heart failure	176 (23)	22 (12)	119 (28)	35 (26)	<0.001
Peripheral vascular disease	121 (16)	17 (9)	79 (18)	25 (19)	0.01
Cerebrovascular disease	154 (21)	24 (13)	105 (24)	25 (19)	0.005
Dementia	92 (12)	8 (4)	71 (16)	13 (10)	<0.001
Chronic obstructive pulmonary disease	148 (20)	35 (20)	83 (19)	30 (22)	0.69
Connective tissue disease	9 (1)	4 (22)	5 (12)	0 (0)	0.21
Peptic ulcer disease	102 (14)	12 (6)	65 (15)	25 (19)	0.003
Hemiplegia	11 (1)	0 (0)	4 (0.9)	2 (1)	0.10
Liver disease	63 (8)	14 (8)	31 (7)	18 (13)	0.07

(*Continued*)

Table 1 (Continued).

	Total Cohort (N=750, 100%) n (%)	Community-Acquired (N=185, 25%), n (%)	Healthcare-Associated (N=431, 57%), n (%)	Hospital-Acquired (N=134, 18%) n (%)	*P*-value
Renal dialysis	127 (17)	0 (0)	112 (26)	15 (11)	<0.001
History of malignancy	147 (20)	18 (10)	93 (22)	36 (27)	<0.001
HIV	27 (4)	7 (4)	16 (4)	4 (3)	0.91
Solid organ transplant	7 (0.9)	0 (0)	7 (2)	0 (0)	
Charlson score					
(median; IQ1, IQ3)	2 (1, 4)	1 (0, 3)	3 (1, 4)	3 (1, 4)	0.002
(range)	(0–12)	(0–9)	(0–11)	(0–12)	
Tobacco use ongoing	192 (26)	63 (34)	90 (21)	39 (29)	0.002
Alcohol use ongoing	113 (15)	42 (23)	43 (10)	28 (21)	<0.001
Infection risks					
AICD or Pacemaker present at admission	42 (6)	4 (2)	31 (7)	7 (5)	0.04
Documented decubitus at admission	123 (17)	23 (13)	83 (20)	17 (13)	0.04
Intravascular catheter present at admission	195 (26)	0 (0)	146 (34)	49 (37)	<0.001
Hemodialysis catheter	123 (31)	0 (0)	104 (42)	19 (24)	
PICC line	30 (8)	0 (0)	17 (7)	13 (17)	
Central venous catheter	21 (5)	0 (0)	7 (3)	14 (18)	
Port	19 (5)	0 (0)	17 (7)	2 (3)	
Urinary catheter present at admission	80 (11)	0 (0)	58 (14)	22 (16)	<0.001
PEG present at admission	50 (7)	0 (0)	35 (8)	15 (11)	<0.001
History of resistant organism					<0.001
MRSA	55 (8)	3 (2)	39 (9)	13 (10)	
VRE	6 (0.8)	0 (0)	2 (0.4)	4 (3)	
Hospitalization characteristics					
Admitting service					0.002
Medicine	665 (89)	169 (92)	389 (90)	107 (80)	
Surgery	35 (5)	8 (4)	13 (3)	14 (10)	
Ob/Gyn	8 (1)	0 (0)	3 (0.7)	5 (4)	
Pediatrics	1 (0.1)	0 (0)	0 (0)	1 (0.7)	
Psychiatry	1 (0.1)	1 (0.5)	3 (0.7)	1 (0.7)	
Urology	5 (0.7)	1 (0.5)	3 (0.7)	1 (0.7)	
Orthopedics	5 (0.7)	5 (2)	20 (5)	5 (4)	
Other	30 (4)				
Admission source					<0.001
Home	542 (72)	181 (98)	275 (64)	86 (64)	
Nursing Home	162 (22)	0 (0)	144 (33)	18 (13)	
Rehab	11 (1)	0 (0)	7 (2)	4 (3)	
Other Hospital	25 (3)	0 (0)	0 (0)	25 (19)	
Hospitalized in prior 12 months	415 (55)	0 (0)	346 (81)	69 (51)	<0.001
If yes, same hospital?	384 (51)	0 (0)	324 (75)	60 (45)	<0.001

Note: *Comparisons were made between each location of acquisition designation and the total cohort.

BSIs in community to tertiary care hospitals and investigated the role of location of acquisition. In a study from Switzerland comparing BSIs in community and tertiary care hospitals over a 7-year time period, investigators found that *E. coli and S. aureus* BSIs were more common in community hospitals, while community-acquired polymicrobial BSIs and community acquired coagulase-negative staphylococcal BSIs were more common in tertiary care hospitals.[12] A study of Spanish hospitals revealed that a respiratory tract source of BSI was more common in community hospitals compared to skin and skin structure sources of BSI in tertiary care hospitals.[13] Interestingly, when evaluating location of acquisition, the investigators noted no cases of community-acquired MRSA BSI in either community or

Table 2 Clinical Outcomes*

	Total Cohort (N=750, 100%) n (%)	Community-Acquired (N=185, 25%) n (%)	Healthcare-Associated (N=431, 57%) n (%)	Hospital-Acquired (N=134, 18%) n (%)	*P*-value
Within week following BSI					
Admitted to ICU	225 (30)	61 (33)	104 (24)	60 (45)	<0.001
CVC placed	197 (26)	43 (23)	108 (25)	46 (35)	0.06
Intubated	107 (14)	28 (15)	40 (9)	39 (29)	<0.001
On pressors	97 (13)	22 (12)	48 (11)	27 (20)	0.02
Procedure performed for BSI					0.002
I&D	59 (8)	16 (9)	34 (8)	9 (7)	
Prosthesis removal	9 (1)	0 (0)	7 (2)	2 (2)	
Other surgery	52 (7)	1 (0.6)	45 (11)	6 (5)	
Pacemaker/AICD removal	1 (0.1)	0 (0)	1 (0.2)	0 (0)	
Percutaneous drain placed	2 (0.2)	0 (0)	2 (0.4)	0 (0)	
Total duration of hospitalization	8	7	7	23	
(median; IQ1, IQ3)	(4, 14)	(3, 10)	(4, 12)	(12, 39)	
(range)	0–161	0–69	0–78	3–161	<0.001
PICC placed for outpatient IV antibiotics	79 (11)	16 (9)	50 (12)	13 (10)	0.54
Died in the Hospital	148 (20)	17 (9)	95 (22)	36 (27)	<0.001
Discharge status					<0.001
Home	308 (41)	107 (58)	166 (39)	35 (26)	
Home Health	51 (7)	14 (8)	23 (5)	14 (10)	
Rehab	36 (5)	11 (6)	16 (4)	9 (7)	
Nursing Home	139 (19)	10 (5)	98 (23)	31 (23)	
Tertiary care hospital	52 (7)	19 (10)	28 (6)	5 (4)	
AMA	3 (0.4)	1 (0.5)	1 (0.2)	1 (0.7)	
Other	11 (1)	4 (2)	4 (0.9)	3 (2)	
Readmitted within 90 days	212 (28)	34 (18)	138 (32)	40 (30)	0.002

Note: *Comparisons were made between each location of acquisition designation and the total cohort.

tertiary-care hospital compared to the present study where MRSA BSI accounted for 19% of cases of community-acquired gram-positive BSI. This discrepancy in findings points to the varying epidemiology of BSI pathogens between the community and tertiary-care hospital settings as well as the likely impact of geographic location on epidemiology.

Clinical microbiology expertise, rapid molecular diagnostic testing, antimicrobial stewardship programs, and even infectious diseases subspecialty consultation may not be readily available in the community hospital setting. A growing body of literature on epidemiology of BSIs in community hospitals could help providers identify patient populations at risk and guide early, appropriate antimicrobial selection. For example, the finding that MSSA and MRSA are the most common infecting pathogens in this cohort could guide early empiric anti-staphylococcal antimicrobial therapy in a patient in whom the provider suspects a gram-positive BSI.

In the present study, only 43% of the cohort received appropriate antibiotics within 24 hours for gram-positive BSI, and 80% ultimately received appropriate antibiotics at some point during the hospitalization. These findings may be due to treating providers underestimating the possibility of the patient presenting with a *S. aureus* or even an MDRO at the time of BSI presentation. In fact, 31% of gram-positive BSIs in this cohort were due to MDROs such as MRSA or methicillin-resistant coagulase negative *Staphylococcus*. In support of this finding, a previous study has shown that only half of the patients in community hospitals with MRSA BSI receive appropriate, empirical therapy within 24 hours of the first positive blood culture for MRSA.[14]

Location of acquisition of gram-positive BSI did impact receipt of appropriate antibiotics within 24 hours with hospital-acquired BSI being an independent risk factor. This finding corresponds to a previous report of patients presenting with gram-negative BSI in community hospitals where patients with healthcare-associated or hospital-acquired BSI

Table 3 Infection Data*

	Total Cohort (N=750, 100%) n (%)	Community-Acquired (N=185, 25%) n (%)	Healthcare-Associated (N=431, 57%) n (%)	Hospital-Acquired (N=134, 18%) n (%)	*P*-value
BSI Data					
Type of BSI					0.02
Primary	619 (83)	141 (76)	369 (86)	109 (81)	
Secondary	131 (17)	44 (24)	62 (14)	25 (19)	0.008
Urine	28 (21)	5 (11)	15 (23)	8 (32)	
Wound	28 (21)	7 (16)	19 (30)	2 (8)	
LRTI	47 (35)	25 (56)	16 (25)	12 (24)	
Other	29 (22)	8 (18)	12 (19)	9 (36)	
In ICU prior to BSI	57 (8)	0 (0)	9 (2)	48 (36)	<0.001
In ICU at time of BSI	152 (23)	37 (22)	62 (17)	53 (42)	<0.001
Central line present at time of BSI	190 (26)	0 (0)	128 (31)	62 (47)	<0.001
Organism					<0.001
MRSA	192 (26)	20 (11)	134 (31)	38 (28)	
MSSA	209 (28)	51 (28)	127 (29)	31 (23)	
Coagulase-Negative *Staphylococcus*	135 (18)	17 (9)	76 (18)	42 (31)	
Enterococcus	29 (4)	4 (2)	17 (4)	8 (6)	
	VRE=4	VRE=0	VRE=2	VRE=2	
Group B Streptococci	42 (6)	18 (10)	22 (5)	2 (1)	
Group A Streptococci	15 (2)	8 (4)	6 (1)	1 (0.7)	
Viridans group Streptococci	8 (1)	3 (2)	4 (0.9)	1 (0.7)	
Other Streptococci	114 (15)	64 (35)	42 (10)	8 (6)	
Peptostreptococcus	2 (0.2)	0 (0)	1 (0.2)	1 (0.7)	
Multidrug-Resistant Gram-positive	235 (31)	27 (15)	159 (37)	49 (37)	<0.001
Multidrug-Resistant MRSA	185 (25)	19 (10)	129 (30)	37 (28)	<0.001
Multidrug-Resistant Coagulase-negative *Staphylococcus*	50 (7)	8 (4)	30 (7)	12 (9)	0.24
Polymicrobial	21 (3)	0 (0)	16 (4)	5 (4)	0.03
APACHE score at time of BSI	14	13	15	14	0.28
(median; IQ1, IQ3)	(11, 17)	(10, 15)	(12, 18)	(10, 17)	
(range)	4–30	5–25	4–30	4–30	

Note: *Comparisons were made between each location of acquisition designation and the total cohort.

Table 4 Appropriate Antibiotics*

	Total Cohort (N=750, 100%) n (%)	Community-Acquired (N=185, 25%) n (%)	Healthcare-Associated(N=431, 57%) n (%)	Hospital-Acquired (N=134, 18%) n (%)	*P*-value
Any appropriate antibiotics	594 (80)	140 (77)	342 (80)	112 (84)	0.39
Appropriate antibiotics within 24 hours of BSI	425 (57)	119 (66)	244 (57)	62 (46)	0.002

Note: *Comparisons were made between each location of acquisition designation and the total cohort.

were significantly less likely to receive appropriate antibiotic therapy within the first 24 hours.[5] Another study reports that risk factors for receiving inappropriate antibiotics include being admitted from a nursing facility, being previously hospitalized within the prior 12 months, and having infection due to a multidrug-resistant gram-positive organism.[10] Of note, these studies are from the same network of hospitals during the same time period as the present study.

In the present study of gram-positive BSIs in community hospitals, distinct clinical risk factors were associated

Table 5 Association Between Clinical Risk Factors, BSI Location of Acquisition, and Selected Outcomes (Adjusted Multivariable Model; in Comparison to Community-Acquired BSI)

Outcomes	HAS BSI	HAQ BSI
ICU Admission within 1 week of BSI	0.61 (0.40–0.91)	1.35 (0.83–2.20)
Intubation within 1 week of BSI	0.61 (0.34–1.10)	1.99 (1.08–3.68)
Need for Pressors	0.71 (0.40–1.29)	1.39 (0.72–2.69)
Procedure for BSI	2.18 (1.17–4.22)	1.17 (0.52–2.63)
Received Appropriate Antibiotics within 24 hours of BSI	0.89 (0.57–1.38)	0.48 (0.28–0.82)
Death during Hospitalization	2.10 (1.17–3.95)	2.54 (1.29–5.12)
Readmission in 90 days	2.11 (1.39–3.26)	1.91 (1.13–3.24)

with location of acquisition. Dementia, congestive heart failure, cerebrovascular disease, dialysis dependence, and impaired functional status based on needing assistance with activities of daily living were significantly more common in patients who had healthcare-associated infections. Importantly, patients with healthcare-associated and hospital-acquired infections were significantly more likely to die during the hospitalization. This finding is similar to the report of another multicenter study comparing the epidemiology of healthcare-associated and community-acquired BSIs in tertiary-care hospitals in the US where patients with healthcare-associated BSI had a significantly higher risk of in-hospital mortality compared to patients with community-acquired BSI.[15]

Limitations to the present study include the time elapsing between data collection and data presentation and lack of reporting of microbiologic methods utilized by the nine community hospitals participating in this study. The epidemiology of certain organisms has likely changed in community hospitals similar to that of academic hospitals with increasing rates of MRSA and VRE.[16,17] Additionally, since the creation of this initial community hospital cohort, the US healthcare system has seen increases in *S. aureus* prosthetic device-associated infections and rates of infective endocarditis related to the opioid epidemic.[18,19]

Another limitation of this study is that we did not collect information on microbiologic methods utilized by the nine participating community hospitals. Microbiological methods for detection, identification, and susceptibility testing may influence the management and treatment of BSI. Since the time of this study, improvements on rapid diagnosis of BSI and susceptibility testing could potentially impact the lack of appropriate antibiotic therapy for MDRO gram-positive infections and the subsequent impact on in-hospital mortality.

Regardless, the present analysis is particularly helpful in understanding the epidemiology of gram-positive BSIs in community hospitals: there are distinct infectious risk factors based on location of acquisition that are associated with specific clinical outcomes, MDROs are common causes of gram-positive BSIs in community hospitals, and that many patients receive inappropriate antibiotic therapy. Despite the lapse in time since original data collection, the present study includes a robust, multicenter cohort of gram-positive BSI in community hospitals to serve as the foundation for future study that incorporates the impact of prosthetic devices and rising rates of infective endocarditis.

The present study establishes the epidemiology of gram-positive BSI in community hospitals in the southeastern US as the majority are due to healthcare-associated MSSA BSI. Notably, 43% of patients did not receive appropriate antibiotic therapy for their gram-positive BSI within the first 24 hours of presentation, which may be due to failure to recognize diagnosis or underestimation of the potential for MDRO infection. Distinguishing location of acquisition in a patient presenting with suspected gram-positive BSI is a critical assessment that should influence empiric treatment patterns.

Data Sharing Statement

Data are stored on a secured Duke University server, and de-identified datasets are available upon request. Please contact Dr. Julia Messina, julia.messina@duke.edu, to request the de-identified dataset.

Ethics Approval

This research was performed in accordance with the Declaration of Helsinki and was approved by the Duke University Institutional Review Board. A waiver of informed consent was obtained through the Duke University Institutional Review Board. This research qualified for a waiver of informed consent as it was deemed as

presenting no more than minimal risk of harm to participants and not involving procedures for which written consent is normally required outside of the research context. Patient data confidentiality and compliance with HIPAA regulations were maintained throughout the conduction of this study.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

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