2009

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Reviewed work(s):
Source: *Infection Control and Hospital Epidemiology*, Vol. 30, No. 11 (November 2009), pp. 1050-1056
Published by: The University of Chicago Press on behalf of The Society for Healthcare Epidemiology of America
Stable URL: http://www.jstor.org/stable/10.1086/606165
Accessed: 07/03/2012 23:42

ORIGINAL ARTICLE

Between Community and Hospital: Healthcare-Associated Gram-Negative Bacteremia among Hospitalized Patients

Jonas Marschall, MD; Victoria J. Fraser, MD; Joshua Doherty, BS; David K. Warren, MD, MPH

OBJECTIVE. Healthcare-associated, community-acquired bacteremia is a subcategory of community-acquired bacteremia distinguished by recent exposure of the patient to the healthcare system before hospital admission. Our objective was to apply this category to a prospective cohort of hospitalized patients with gram-negative bacteremia to determine differences in the epidemiological characteristics, treatment, and outcome of community-acquired bacteremia; healthcare-associated, community-acquired bacteremia; and hospital-acquired bacteremia.

DESIGN. A 6-month prospective cohort study.

SETTING. A 1,250-bed tertiary care hospital.

PATIENTS. Adults hospitalized with gram-negative bacteremia.

RESULTS. Among 250 patients, 160 (64.0%) had bacteremia within 48 hours after admission; 132 (82.5%) of these were considered to have healthcare-associated, community-acquired bacteremia, according to previously published criteria. For patients with healthcare-associated, community-acquired bacteremia, compared with patients with community-acquired bacteremia, malignancies (59 [44.7%] of 132 patients vs 3 [10.7%] of 28 patients; $P = .001$), open wounds at admission (42 [31.8%] vs 3 [10.7%]; $P = .02$), and intravascular catheter–related infections (26 [19.7%] vs 0; $P = .009$) were more frequent and *Escherichia coli* as a causative agent was less frequent (16 [57.1%] vs 33 [25.0%]; $P = .001$). There was no difference between these 2 groups in inadequate empirical antibiotic treatment (36 [27.3%] vs 6 [21.4%]; $P = .5$) and hospital mortality (18 [13.6%] vs 2 [[7.1%]; $P = .5$). Compared with 90 patients with hospital-acquired bacteremia, patients with healthcare-associated, community-acquired bacteremia had a higher Charlson score (odds ratio [OR], 1.31 [95% confidence interval (CI), 1.14–1.49]) but were less likely to have lymphoma (OR, 0.07 [95% CI, 0.01–0.51]), neutropenia (OR, 0.21 [95% CI, 0.07–0.61]), a removable foreign body (OR, 0.08 [95% CI, 0.03–0.20]), or *Klebsiella pneumoniae* infection (OR, 0.26 [95% CI, 0.11–0.62]).

CONCLUSIONS. Many cases of gram-negative bacteremia that occurred in hospitalized patients were healthcare associated. The patients differed in some aspects from patients with community-acquired bacteremia and from those with hospital-acquired bacteremia, but not in mortality.

Infect Control Hosp Epidemiol 2009; 30:1050-1056

The distinction between community- and hospital-acquired infections among hospitalized patients is becoming increasingly blurred. Shorter hospital stays, increased outpatient delivery of care, and a rising number of immunocompromised patients in the community account for some of these changes.[1,2] In many cases, the definition of community acquisition does not reflect the increasing number of patients who were exposed to the healthcare system before being admitted to the hospital. Although the difference between community- and hospital-acquired bacteremia has been studied previously,[3] the Centers for Disease Control and Prevention definitions of nosocomial infections do not account for healthcare-associated, community-acquired bacteremia (referred to hereafter as healthcare-associated bacteremia),[4] and they maintain the dichotomous concept of community versus hospital acquisition. This has led to calls for a revised classification of bloodstream infections.[5]

In 2002, Friedman and colleagues proposed a new classification of community-acquired bloodstream infections and established the use of the term healthcare-associated bloodstream infection. Applying a set of 4 criteria, they found many similarities between patients with healthcare-associated infection and those with hospital-acquired infection, in terms of comorbid conditions, sources of infection, presence of microbial pathogens, and susceptibility patterns.[6] They argued that empirical antibiotic treatment should be tailored according to this classification. Since then, few published articles have scrutinized the new classification.[7-10] Shorr et al used a large US database to test the new classification retrospectively in bacterial and fungal bloodstream infections,[8] whereas Les-

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Received March 18, 2009; accepted June 3, 2009; electronically published October 2, 2009.

 0899-823X/2009/3011-0004$15.00. DOI: 10.1086/606165

ens et al and Liao et al restricted their studies to healthcare-associated *Staphylococcus aureus* bacteremia.[7,10] More recently, other terms have been proposed to reflect the circumstances of the acquisition of infection, such as community-acquired healthcare-associated infection[11] or community-onset healthcare-associated infection.[12]

Our objective was to apply the definition by Friedman and colleagues of "healthcare association" to a prospective cohort of hospitalized patients with gram-negative bacteremia, to determine differences in the epidemiological characteristics, treatment, and outcome of community-acquired bacteremia, healthcare-associated bacteremia, and hospital-acquired bacteremia.

METHODS

Setting

Barnes-Jewish Hospital, a 1,250-bed teaching hospital, is the largest hospital in Missouri and has a referral base that includes the St Louis metropolitan area, eastern Missouri, and western Illinois. It houses all medical specialties, including a bone marrow transplantation unit. It is affiliated with Washington University School of Medicine.

Study Design

We performed a 6-month, prospective cohort study of patients with gram-negative bacteremia from August 1, 2006, through January 31, 2007. We received daily electronic notification of all patients with blood cultures positive for any organism on a list of specified gram-negative bacilli. The automated query was run on a daily basis through the Barnes-Jewish Hospital Medical Informatics database, and results were sent daily to 1 of the investigators (J.M.).

Inclusion and Exclusion Criteria

All adult patients admitted to acute care wards who presented with or developed gram-negative bacteremia were included. Patients were considered to have gram-negative bacteremia if they had least 1 positive culture result; if patients had more than 1 bacteremia episode, only the first episode was used for this analysis. Polymicrobial infections were also included. Patients who were bacteremic as outpatients (in clinics or in the emergency department) and who were sent home before a blood culture returned positive results were excluded because we could not determine with certainty the treatment that these patients received.

Data Collection

Paper and electronic medical records were reviewed for demographic information, medical history, home medications, vital signs, microbiological information, diagnostic and therapeutic procedures, and antimicrobial medication. All of these sources were reviewed daily during the hospital stay. Special attention was given to 2 areas of information: To determine the adequacy of antibiotic therapy, microbiological information was entered sequentially as time blood sample was obtained, time of notification of positive culture and Gram stain results, time of identification of microorganism, and time of notification of antibiotic susceptibilities. Start and stop dates and times for the use of each antibiotic were entered sequentially.

Charlson comorbidity[13] and McCabe severity of illness[14] scores at admission were determined. The key clinical outcomes measured included the development of sepsis and hypotension, the subsequent transfer to the intensive care unit, length of hospital stay after detection of positive blood culture results, and in-hospital mortality.

Definitions

Sepsis and sepsis-induced hypotension were defined according to established criteria.[15] Inadequate empirical antibiotic treatment was defined as either no antibiotic administered or no antibiotic administered to which all bacteria were susceptible within 24 hours after blood sample was obtained.[16]

Patients received a diagnosis of community-acquired, gram-negative bacteremia if their first positive blood culture results were obtained from blood samples drawn within 48 hours after hospital admission.[3] Cases of community-acquired bacteremia were further classified as being healthcare associated if 1 or more of the following criteria were present: outpatient treatment, hemodialysis, or intravenous chemotherapy during the past 30 days; hospitalization for at least 2 days during the past 90 days; home intravenous therapy or wound care during the past 30 days; or residence in a long-term care facility.[6]

Data Analysis and Statistical Methods

Data entry was performed with Microsoft Access and Excel (Microsoft). Data were analyzed with SPSS, version 14 (SPSS).

Univariate comparisons among categorical variables were performed by use of the χ^2 test or the Fisher exact test as appropriate. Comparisons among continuous independent variables were performed by use of the Student t test or the Mann-Whitney U test as appropriate. Variables found to have a P value of less than .1 on univariate testing were considered for entry into a forward, stepwise multivariate logistic regression model. Multivariate analysis was applied to the comparison of healthcare-associated bacteremia and hospital-acquired bacteremia, but because of the small numbers, a multivariate analysis could not be applied to the comparison of healthcare-associated bacteremia and community-acquired bacteremia (ie, bacteremia in patients without any known healthcare exposure). A 2-sided P value of less than .05 was considered to indicate a statistically significant difference. The study was approved by the Washington University Human Research Protection Office.

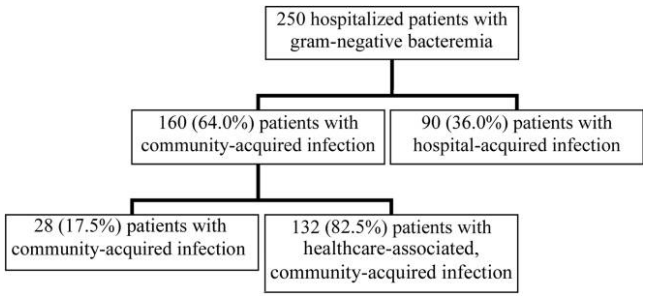

FIGURE 1. Differentiation of hospitalized patients with gram-negative bacteremia, according to method of acquisition.

RESULTS

Frequency of Healthcare-Associated Infection among Hospitalized Patients with Gram-Negative Bacteremia

We included 250 hospitalized patients with gram-negative bacteremia in our study (Figure). One hundred sixty (64.0%) of them had community-acquired bacteremia, and 90 (36.0%) had hospital-acquired bacteremia. Overall, 207 patients (82.8%) in the cohort had prior exposure to the healthcare system.

Among the subset of 160 patients with bacteremia within 48 hours after admission, 132 (82.5%) had healthcare-associated bacteremia, and 28 (17.5%) had community-acquired bacteremia. Of the 90 patients with hospital-acquired bacteremia, 75 (83.3%) had prior exposure to the healthcare system.

For the 132 patients with healthcare-associated bacteremia, we examined the 4 criteria that define healthcare association (Table 1). The criterion most frequently present was outpatient treatment, hemodialysis, or intravenous chemotherapy (ie, 102 [77.3%] of 132 patients). Forty patients (30.3%) received a diagnosis of healthcare-associated infection on the basis of 1 criterion, 67 patients (50.8%) on the basis of 2 criteria, 19 patients (14.4%) on the basis of 3 criteria, and 6 patients (4.5%) on the basis of all 4 criteria.

Comparison of Healthcare-Associated Bacteremia and Community-Acquired Bacteremia

Compared with patients with community-acquired bacteremia (Table 2), patients with healthcare-associated bacteremia were older (mean ± standard deviation, 57.9 ± 15.8 years vs 54.5 ± 20.4 years; $P = .046$), had a higher Charlson score (median [range], 4 [0–16] vs 1 [0–15]; $P = .005$), and were more severely ill (mean McCabe score, 1.54 vs 1.25; $P = .02$). Malignant tumors were more frequent among the 132 patients with healthcare-associated bacteremia than they were among the 28 patients with community-acquired bacteremia (59 [44.7%] vs 3 [10.7%]; $P = .001$), as were skin wounds at admission (42 [31.8%] vs 3 [10.7%]; $P = .02$) or the presence of a removable foreign body at the time of infection (69 [52.3%] vs 8 [28.6%]; $P = .02$). Compared with patients with community-acquired bacteremia, for patients with healthcare-associated bacteremia, the urinary tract was less frequently the source of infection (38 [28.8%] vs 16 [57.1%]; $P = .004$), intravascular catheters were a more common source of infection (26 [19.7%] vs 0; $P = .009$), and *Escherichia coli* (monomicrobial bacteremia) was less frequently involved (33 [25.0%] vs 16 [57.1%]; $P = .001$).

There was no significant difference in the administration of inadequate empirical antibiotic treatment (36 [27.3%] healthcare-associated cases vs 6 [21.4%] community-acquired cases; $P = .5$), in transfer to the intensive care unit (46 [34.8%] vs 5 [17.9%]; $P = .08$), in length of hospital stay after the positive blood culture sample was obtained (median, 5.5 [range, 0–89.3] vs 4.2 [0–34.6] days; $P = .09$), or in in-hospital mortality (18 [13.6%] vs 2 [7.1%]; $P = .5$) (Table 2).

Comparison of Healthcare-Associated Bacteremia and Hospital-Acquired Bacteremia

Compared with patients with hospital-acquired bacteremia, patients with healthcare-associated bacteremia (Table 3) had a lower severity of illness (mean McCabe score, 1.54 vs 1.76; $P = .04$). Lymphoma was less frequent among the 132 patients with healthcare-associated bacteremia than it was among the 90 patients with hospital-acquired bacteremia (2 [1.5%] vs 13 [14.4%]; $P < .001$), as was leukemia (8 [6.1%] vs 19 [21.1%]; $P = .001$), neutropenia prior to the bacteremia (9 [6.8%] vs 27 [30.0%]; $P < .001$), mucositis (6 [4.5%] vs 15 [16.7%]; $P = .002$), and the presence of a removable foreign body (69 [52.3%] vs 81 [90.0%]; $P < .001$). Conversely, metastatic solid tumors were more frequent among patients with healthcare-associated bacteremia than they were among patients with hospital-acquired bacteremia (27 [20.5%] vs 4 [4.4%]; $P = .001$), as was dementia (14 [10.6%] vs 1 [1.1%]; $P = .006$).

Compared with patients with hospital-acquired bacteremia, for patients with healthcare-associated bacteremia, the source of infection was more often the urinary tract (38 [28.8%] vs 13 [14.4%]; $P = .01$) and remained less frequently unknown (27 [20.5%] vs 32 [35.6%]; $P = .01$). *E. coli* was more com-

TABLE 1. Frequency of the 4 Criteria That Define Healthcare Association among 132 Patients with Healthcare-Associated, Community-Acquired Bacteremia

Criterion	No. (%) of patients[a]
Outpatient treatment, hemodialysis, intravenous chemotherapy in the past 30 days	102 (77.3)
Hospitalization for >1 day in the past 90 days	95 (72.0)
Intravenous therapy or wound care at home in the past 30 days	32 (24.2)
Residence in long-term care facility	26 (19.7)

[a] More than 1 criterion can be present in a single patient; therefore, the total exceeds 132.

TABLE 2. Comparison of 160 Hospitalized Patients with Community-Acquired Gram-Negative Bacteremia

Variable	Patients with healthcare-associated, community-acquired bacteremia (n = 132)	Patients with community-acquired bacteremia (n = 28)	P
Age, years, mean ± SD	57.9 ± 15.8	54.5 ± 20.4	.046
Male sex	69 (52.3)	9 (32.1)	.05
Body mass index, median (range)	26.4 (13.3–66.4)	28.9 (16.8–70.4)	.2
Charlson score			
Mean	4.8	3.2	.005
Median (range)	4 (0–16)	1 (0–15)	
McCabe score			
Mean	1.54	1.25	.02
Median (range)	1 (1–3)	1 (1–3)	
Comorbidities			
Congestive heart failure	19 (14.4)	2 (7.1)	.5
Chronic pulmonary disease	25 (18.9)	3 (10.7)	.4
Malignant tumor	59 (44.7)	3 (10.7)	.001
Lymphoma	2 (1.5)	0	>.99
Leukemia	8 (6.1)	0	.4
Metastatic solid tumor	27 (20.5)	3 (10.7)	.2
Diabetes mellitus	49 (37.1)	13 (46.4)	.4
Cerebrovascular disease	19 (14.4)	2 (7.1)	.5
Dementia	14 (10.6)	1 (3.6)	.5
Hemiplegia	8 (6.1)	0	.4
Moderate or severe liver disease	8 (6.1)	1 (3.6)	>.99
Neutropenia	9 (6.8)	0	.4
Renal insufficiency[a]	42 (31.8)	7 (25.0)	.5
Hyperglycemia[b]	22 (16.7)	7 (25.0)	.3
Mucositis	6 (4.5)	0	.6
Skin wound at admission	42 (31.8)	3 (10.7)	.02
Skin incision at admission	16 (12.1)	0	.08
Removable foreign body present[c]	69 (52.3)	8 (28.6)	.02
Source of infection			
Urinary tract	38 (28.8)	16 (57.1)	.004
Intravascular catheter	26 (19.7)	0	.009
Gastrointestinal or hepatobiliary system	22 (16.7)	4 (14.3)	>.99
Unknown	27 (20.5)	6 (21.4)	.9
Causative microorganism			
Escherichia coli	33 (25.0)	16 (57.1)	.001
Klebsiella pneumoniae	20 (15.2)	2 (7.1)	.3
Pseudomonas aeruginosa	9 (6.8)	0	.4
Multidrug-resistant organism[d]	7 (5.3)	0	.6
Outcome measures			
Inadequate empirical antibiotic treatment	36 (27.3)	6 (21.4)	.5
Sepsis	118 (89.4)	25 (89.3)	>.99
Sepsis-induced hypotension	62 (47.0)	8 (28.6)	.8
Transfer to intensive care unit	46 (34.8)	5 (17.9)	.08
Postbacteremia length of hospital stay, median (range), days	5.5 (0–89.3)	4.2 (0–34.6)	.09
In-hospital death	18 (13.6)	2 (7.1)	.5

NOTE. Data are no. (%) of patients unless otherwise indicated. SD, standard deviation.

[a] Creatinine level, >1.5 mg/dL.

[b] Glucose level, >200 mg/dL.

[c] At the time when the blood sample was obtained for the first culture that returned positive results.

[d] Resistance to cephalosporins, aminoglycosides, and fluoroquinolones.[17]

TABLE 3. Comparison of 222 Hospitalized Patients with Gram-Negative Bacteremia That Is Associated with Exposure to the Healthcare System (Including Multivariate Analysis)

Variable	Patients with healthcare-associated, community-acquired bacteremia (n = 132)	Patients with hospital-acquired bacteremia (n = 90)	P	OR (95% CI)
Age, years, mean ± SD	57.9 ± 15.8	54.9 ± 15.1	.2	
Male sex	69 (52.3)	48 (53.3)	.9	
Body mass index, median (range)	26.4 (13.3–66.4)	26.2 (14.6–59.9)	>.99	
Charlson score				1.31 (1.14–1.49)
Mean	4.8	3.7	.05	
Median (range)	4 (0–16)	4 (0–12)		
McCabe score				
Mean	1.54	1.76	.04	
Median (range)	1 (1–3)	2 (1–3)		
Comorbidities				
Congestive heart failure	19 (14.4)	9 (10.0)	.3	
Chronic pulmonary disease	25 (18.9)	16 (17.8)	.8	
Malignant tumor	59 (44.7)	50 (55.6)	.1	
Lymphoma	2 (1.5)	13 (14.4)	<.001	0.07 (0.01–0.51)
Leukemia	8 (6.1)	19 (21.1)	.001	
Metastatic solid tumor	27 (20.5)	4 (4.4)	.001	
Diabetes mellitus	49 (37.1)	25 (27.8)	.1	
Cerebrovascular disease	19 (14.4)	7 (7.8)	.1	
Dementia	14 (10.6)	1 (1.1)	.006	
Hemiplegia	8 (6.1)	7 (7.8)	.6	
Moderate or severe liver disease	8 (6.1)	2 (2.2)	.2	
Neutropenia	9 (6.8)	27 (30.0)	<.001	0.21 (0.07–0.61)
Renal insufficiency[a]	42 (31.8)	19 (21.1)	.08	
Hyperglycemia[b]	22 (16.7)	12 (13.3)	.5	
Mucositis	6 (4.5)	15 (16.7)	.002	
Skin wound at admission	42 (31.8)	29 (32.2)	.9	
Skin incision at admission	16 (12.1)	7 (7.8)	.3	
Removable foreign body present[c]	69 (52.3)	81 (90.0)	<.001	0.08 (0.03–0.20)
Sources of infection				
Urinary tract	38 (28.8)	13 (14.4)	.01	
Intravascular catheter	26 (19.7)	14 (15.6)	.4	
Gastrointestinal or hepatobiliary system	22 (16.7)	15 (16.7)	>.99	
Unknown	27 (20.5)	32 (35.6)	.01	
Causative microorganism				
Escherichia coli	33 (25.0)	10 (11.1)	.01	
Klebsiella pneumoniae	20 (15.2)	23 (25.6)	.05	0.26 (0.11–0.62)
Pseudomonas aeruginosa	9 (6.8)	10 (11.1)	.3	
Multidrug-resistant organism[d]	7 (5.3)	5 (5.6)	>.99	
Outcome measures				
Inadequate empirical antibiotic treatment	36 (27.3)	37 (41.1)	.03	
Sepsis	118 (89.4)	88 (97.8)	.02	
Sepsis-induced hypotension	62 (47.0)	35 (38.9)	.2	
Transfer to intensive care unit	46 (34.8)	19 (21.1)	.03	
Postbacteremia length of hospital stay, median (range), days	5.5 (0–89.3)	8.0 (0–105.6)	.002	
In-hospital death	18 (13.6)	15 (16.7)	.5	

NOTE. Data are no. (%) unless otherwise indicated. CI, confidence interval; OR, odds ratio; SD, standard deviation. Variables considered for entry in a forward stepwise multivariate logistic regression model included McCabe severity of illness score at admission, Charlson comorbidity score at admission, leukemia, lymphoma, any malignant disease, metastatic solid tumor, neutropenia prior to bacteremia, diabetes mellitus, cerebrovascular disease, source in urinary tract, unknown source of bacteremia, monomicrobial infection with *E. coli*, monomicrobial infection with *K. pneumoniae*, serum creatinine level >1.5 mg/dL at admission, mucositis, and removable foreign body present. The −2 log likelihood value for the final model was 213.745, and the Hosmer-Lemeshow goodness-of-fit χ^2 test value was 12.193 (P = .143).

[a] Creatinine level, >1.5 mg/dL.

[b] Glucose level, >200 mg/dL.

[c] At the time when the blood sample was obtained for the first culture that returned positive results.

[d] Resistance to cephalosporins, aminoglycosides, and fluoroquinolones.[17]

monly the causative pathogen in healthcare-associated infections (33 [25.0%] vs 10 [11.1%]; $P = .01$).

The administration of empirical antibiotic treatment was less often inadequate in cases of healthcare-associated bacteremia than it was in cases of hospital-acquired bacteremia (36 [27.3%] vs 37 [41.1%]; $P = .03$). Sepsis was less frequent in cases of healthcare-associated bacteremia than it was in cases of hospital-acquired bacteremia (118 [89.4%] vs 88 [97.8%]; $P = .02$), and the length of hospital stay after detection of bacteremia was shorter in the former group (median [range], 5.5 [0–89.3] vs 8.0 [0–105.6] days; $P = .002$). Transfer to the intensive care unit more frequently occurred among patients with healthcare-associated bacteremia than it did among patients with hospital-acquired bacteremia (46 [34.8%] vs 19 [21.1%]; $P = .03$). However, there was no significant difference in in-hospital mortality (18 patients [13.6%] with healthcare-associated bacteremia vs 15 patients [16.7%] with hospital-acquired bacteremia; $P = .5$).

In multivariate analysis (Table 3), a higher Charlson score (odds ratio [OR], 1.31 [95% confidence interval {CI}, 1.14–1.49]; $P < .001$) was associated with healthcare-associated bacteremia. Patients with healthcare-associated bacteremia were less likely to have lymphoma (OR, 0.07 [95% CI, 0.01–0.51]; $P = .009$), neutropenia (OR, 0.21 [95% CI, 0.07–0.61]; $P = .004$), a removable foreign body (OR, 0.08 [95% CI, 0.03–0.20]; $P < .001$), or *Klebsiella pneumoniae* infection (OR, 0.26 [95% CI, 0.11–0.62]; $P = .003$) than were patients with hospital-acquired bacteremia.

DISCUSSION

Only a few studies have examined the utility of the new classification of community-acquired bacteremia proposed by Friedman et al.[6] Lesens et al and Liao et al performed prospective studies on *S. aureus* infection,[7,10] and Shorr et al used a large preexisting database to collect information retrospectively on various bloodstream infections.[8]

In our study, the majority of cases of bacteremia (82.5%) that would conventionally be classified as community acquired were in fact healthcare associated. This is higher than the 56.5%–59.5% reported elsewhere.[6,8] In the subgroup of gram-negative bacteria described by Shorr et al, the percentage of bloodstream infections that were healthcare-associated infections was lower than that seen in our study (56.7%). Similarly, Friedman's group reported that 50.9% of their 159 cases of gram-negative bacteremia were healthcare associated.[18] There are several possible explanations for the increased proportion of patients with healthcare-associated infections in our study. As a result of the prospective design of our study, we may have improved the ascertainment of recent exposure to the healthcare system. Although previous studies also included tertiary care centers, factors unique to our setting may have played an additional role (eg, a large population of bone marrow transplant recipients and cancer patients). This is supported by the observation that the majority (63.8%) of patients with healthcare-associated bacteremia in our study had outpatient treatment, hemodialysis, or intravenous chemotherapy during the prior 30 days, compared with only 78 of 186 patients (42%) in an earlier study.[6]

Urinary tract infections were the most common source of community-acquired bacteremia, and they were a less common source in healthcare-associated and hospital-acquired bacteremia. This has been reported elsewhere.[6] *E. coli*, probably the most important pathogen in gram-negative community-acquired infections,[8] followed that trend closely in our population, and the pattern was similar to that in the population of the Shorr et al study. Unlike the work of Shorr et al, however, which included only patients with bacteremia detected during the first 5 days of hospitalization—which might have distorted the epidemiological characteristics of nosocomial pathogens—our data account for the entire hospital stay.

Patients with community-acquired bacteremia were less likely to have malignancies or to have intravascular catheters as a source of bacteremia than those with healthcare-associated bacteremia. Patients with hospital-acquired bacteremia were more likely to have neutropenia or lymphoma than were patients with healthcare-associated bacteremia. In summary, several characteristics distinguish community-acquired bacteremia from healthcare-associated bacteremia and hospital-acquired bacteremia. Our findings therefore justify the reclassification by Friedman et al.[6,10]

Whether the adequacy of empirical antibiotic treatment is an important prognostic factor in bloodstream infections is unclear: some studies show worse outcomes,[19,20] whereas others fail to demonstrate a detrimental effect of inadequate treatment.[16,18] We did not find a difference in the administration of inadequate treatment between healthcare-associated bacteremia and community-acquired bacteremia. Patients with hospital-acquired infections, however, were more likely to receive inadequate treatment, which has been reported elsewhere.[16,19]

We did not find a difference in mortality rates among the 3 groups, however. This is different from the results of previous studies, which reported an increased risk of inadequate treatment for healthcare-associated bacteremia[18] and significantly higher mortality from healthcare-associated bacteremia than from community-acquired bacteremia.[6,8] Shorr and colleagues hypothesized that poor outcome in healthcare-associated infections might be largely due to the *S. aureus* subset, but they did not collect data on adequacy of treatment. Other authors could not detect differences in mortality attributable to *S. aureus* bacteremia among the 3 groups of patients.[7,10] Because Shorr et al did not display separate mortality rates for infections caused by gram-negative organisms, there are no data available for comparison of our findings.

There are a few limitations to our study. First, our study was restricted in terms of the group of microorganisms and in terms of patient selection, by excluding patients not sufficiently ill to be admitted to the hospital. In addition, the

study was performed in a tertiary care center with a large oncology department and distinct empirical prescribing patterns, which might reduce the generalizability of our findings.

Our study demonstrates that there are differences, as well as overlapping areas, in the epidemiological characteristics of community-acquired bacteremia, healthcare-associated bacteremia, and hospital-acquired bacteremia. The category of healthcare-associated bacteremia seems to represent a transitional state between community- and hospital-acquired bacteremia. The original intention of distinguishing healthcare-associated bacteremia from community-acquired bacteremia was to improve empirical treatment of patients at hospital admission. While our study noted differences in the microbiological characteristics of gram-negative pathogens between community-acquired bacteremia and healthcare-associated bacteremia, there was no difference in adequacy of empirical treatment or subsequent outcomes between these 2 types of bacteremia. Although this classification is useful to elicit epidemiological nuances, it remains to be seen whether larger prospective studies will show that the reclassification has an effect on clinical outcomes.

ACKNOWLEDGMENTS

We thank Cherie Hill, Stacy Leimbach, and Dorothy Sinclair for their invaluable data management.

Financial support. J.M. received a research grant from the Swiss National Science Foundation (PBBSB-113014) and is a participant in the TL1 CTSA Postdoctoral Program (K30RR022251). V.J.F. is funded through an NIH grant (5K24 AI 06779402). D.K.W. and V.J.F. received a CDC Prevention Epicenter Program grant (5U 01 CI000033302).

Potential conflicts of interest. D.K.W. reports that he is a consultant for 3M Healthcare and Cardinal Health and receives research funding from Sage Products, 3M Healthcare, bioMérieux, and Cubist Pharmaceuticals. V.J.F. reports that she has been a consultant for Merck and a member of the speakers' bureau for Pfizer, Merck, and Cubist Pharmaceuticals in the past 3 years. All other authors report no conflicts of interest relevant to this article.

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