Risk Factors for Mortality in Patients with Persistent *Staphylococcus aureus* Bacteremia

Eunmi Yang,[1] Hyemin Chung,[1] Yoonyo Lee[1], Eunsil Kim[2], Jiwon Jung,[1] Min Jae Kim,[1] Yong Pil Chong,[1] Sung-Han Kim,[1] Sang-Oh Lee,[1] Sang-Ho Choi,[1] and Yang Soo Kim [1,2]†

[1]Division of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
[2]Center for Antimicrobial Resistance and Microbial Genetics, University of Ulsan College of Medicine, Seoul, Republic of Korea

Contact information
Yang Soo Kim, MD, PhD
Division of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea
Tel: +82-2-3010-3303,
E-mail: yskim@amc.seoul.kr

Background

Staphylococcus aureus bacteremia (SAB) is a leading cause of bacteremia and persistent SAB is associated with poor outcomes. We evaluated clinical characteristics, microbiologic, genotypic characteristics, and risk factors for 30-day mortality with persistent *S. aureus* bacteremia.

Methods

We reviewed patients enrolled in a prospective cohort of adult patients with *S. aureus* bacteremia at a tertiary hospital from August 2008 to December 2018. Clinical characteristics, outcomes, and microbiologic characteristics of patients with persistent bacteremia (≥ 3 d) were evaluated.

Results

Of the total 969 patients, 617 (63.7%) patients had persistent bacteremia. The median duration of bacteremia with persistent bacteremia was 5 days. The most common sources of persistent bacteremia were central venous catheter-related infection (33.4%) and bone and joint infection (14.9%). Methicillin resistant *S. aureus* (MRSA) isolates were analyzed in 372 (60.3%) patients and metastatic infections were 217 (35.2%) with persistent bacteremia. In the multivariate analysis, APACHE Ⅱ score (adjusted odds ratio [aOR], 1.07; 95% confidence interval [CI], 1.03–1.10), Charlson comorbidity index score (aOR, 1.14; 95% CI, 1.04–1.25), liver cirrhosis (aOR, 2.47; 95% CI, 1.44–4.23), and *S. aureus* pneumonia (aOR, 3.04; 95% CI, 1.29–7.18) were independently associated with 30-d mortality. In persistent MRSA bacteremia, ST5-SCC*mec*Ⅱ was 59.7% (222/372) and *agr* dysfunction was 64.8% (241/372). After adjusting for confounding factors, APACHE Ⅱ score (aOR, 1.08; 95% confidence interval [CI], 1.04–1.13), liver cirrhosis (aOR, 3.48; 95% CI, 1.72–7.02), *S. aureus* pneumonia (aOR, 4.45; 95% CI, 1.40–14.12), and vancomycin MIC 1.5 mg/L (aOR, 2.16; 95% CI, 1.15–4.04) were independently associated with 30-d mortality.

Conclusion

In persistent *S. aureus* bacteremia, clinical factors, including APACHE Ⅱ score, Charlson comorbidity index score, liver cirrhosis, and *S. aureus* pneumonia contribute to 30-d mortality.

Table 1. Demographic and Clinical characteristics of Patients with Persistent *S. aureus* Bacteremia

Characteristic	Deceased patients (n = 113)	Surviving patients (n = 504)	*p* value
Age (yr), median (IQR)	64 (53.5–72.5)	63 (53–71)	0.14
Male	63 (55.8)	319 (63.3)	0.14
Place of acquisition			
CA-NHCA	12 (10.6)	100 (19.8)	0.02
CA-HCA	34 (30.1)	153 (30.4)	0.96
Hospital-acquired	67 (59.3)	251 (49.8)	0.07
Underlying disease			
Diabetes mellitus	31 (27.4)	177 (35.1)	0.12
Solid tumor	47 (41.6)	165 (32.7)	0.07
Liver cirrhosis	31 (27.4)	62 (12.3)	<0.01
End state renal disease	10 (8.8)	72 (14.3)	0.12
Hypertension	45 (39.8)	222 (44.0)	0.41
Cardiovascular disease	13 (11.5)	43 (8.5)	0.32
Hematologic malignancy	10 (8.8)	39 (7.7)	0.69
Prior antibiotic use within 1 mo	54 (47.8)	205 (40.7)	0.17
Methicillin-resistant isolate	67 (59.3)	305 (60.5)	0.81
Charlson comorbidity index, median (IQR)	4 (2–6)	2 (1–4)	<0.01
APACHE Ⅱ, median (IQR)	19 (15–23)	15 (11–19)	<0.01
Pitt bacteremia score, median (IQR)	1 (0–3)	1 (0–2)	0.03
Septic shock	18 (15.9)	47 (9.3)	0.04
Central venous catheter	46 (40.7)	209 (41.5)	0.88
Prosthetic device	18 (15.9)	115 (22.8)	0.11
Characteristics of infection			
CVC-related infection	35 (31.0)	171 (33.9)	0.55
Removal of CVC	32/35 (91.4)	166/171 (97.1)	0.14
Bone and joint infection	14 (12.4)	78 (15.5)	0.41
Primary bacteremia	13 (11.5)	58 (11.5)	>0.99
Skin and soft tissue	7 (6.2)	41 (8.1)	0.49
Infective endocarditis	8 (7.1)	32 (6.3)	0.78
Surgical site infection	7 (6.2)	23 (4.6)	0.47
Pneumonia	13 (11.5)	13 (2.6)	<0.01
Peripheral catheter-related infection	7 (6.2)	17 (3.4)	0.18
Metastatic infection	35 (31.0)	182 (36.1)	0.30
Lung (septic pneumonia)	9 (8.0)	56 (11.1)	0.33
Skin and soft tissue	5 (4.4)	56 (11.1)	0.03
Bone and joint	6 (5.3)	44 (8.7)	0.23
Central nervous system	11 (9.7)	28 (5.6)	0.10
Eye (endophthalmitis)	8 (7.1)	30 (6.0)	0.65
Cardiac valve (endocarditis)	5 (4.4)	15 (3.0)	0.39
Eradicable focus	56 (49.6)	295 (58.5)	0.08
Removal of eradicable focus	49/56 (87.5)	270/295 (91.5)	0.34

Table 2. Multivariate Analysis of Risk Factors for 30-d Mortality with Persistent *S. aureus* Bacteremia

Characteristic	Univariate analysis			Multivariate analysis[a]	
	Deceased patients (n = 113)	Surviving patients (n = 504)	*p* value	Odds ratio (95% CI)	*p* value
Age, median (IQR)	64 (53.5–72.5)	63 (53–71)	0.14		
APACHE Ⅱ, median (IQR)	19 (15–23)	15 (11–19)	<0.01	1.07 (1.03–1.10)	<0.01
Bone and joint infection	14 (12.4)	78 (15.5)	0.41		
Charlson comorbidity index, median (IQR)	4 (2–6)	2 (1–4)	<0.01	1.14 (1.04–1.25)	0.01
CA-NHCA	12 (10.6)	100 (19.8)	0.02		
Diabetes mellitus	31 (27.4)	177 (35.1)	0.12		
Liver cirrhosis	31 (27.4)	62 (12.3)	<0.01	2.47 (1.44–4.23)	<0.01
Metastatic bone and joint infection	6 (5.3)	44 (8.7)	0.23		
Metastatic skin and soft tissue	5 (4.4)	56 (11.1)	0.03	0.38 (0.14–1.00)	0.05
Methicillin-resistant isolate	67 (59.3)	305 (60.5)	0.81		
Pneumonia	13 (11.5)	13 (2.6)	<0.01	3.04 (1.29–7.18)	0.01
Prosthetic device	18 (15.9)	115 (22.8)	0.11		

[a] This model fit the data well in terms of discrimination (C-statistic 0.719) and calibration (Hosmer-Lemeshow goodness-of-fit statistic 8.984; P = 0.344)

Table 3. Microbiologic Characteristics and Clinical Management of Patients with Persistent MRSA Bacteremia

Characteristic	Deceased patients (n = 67)	Surviving patients (n = 305)	*p* value
Vancomycin MIC by BMD			
≤1.0 mg/L	44 (65.7)	225 (73.8)	0.18
1.5 mg/L	23 (34.3)	69 (22.6)	0.04
≥2.0 mg/L	0	11 (3.6)	0.23
Vancomycin trough level <15mg/L	22/45 (48.9)	135/264 (51.1)	0.78
Vancomycin trough level (mg/L), median (IQR)	16 (10.3–26)	15 (10–20.4)	0.17
Vancomycin trough level/MIC, median (IQR)	11 (5.8–18.3)	9 (5.5–15.3)	0.31

MIC, Minimum inhibitory concentration; BMD, broth microdilution method

IQR, interquartile range; CA-NHCA, community-acquired, nonhealthcare-associated; CA-HCA, community-acquired, healthcare associated; MRSA, methicillin-resistant *Staphylococcus aureus*, APACHE II, acute physiology and chronic health evaluation II; CVC, central venous catheter; SAB, *Staphylococcus aureus* bacteremia