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ARTICLE

Clinical significance of *Staphylococcus aureus* bacteremia in patients with liver cirrhosis

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Abstract Patients with liver cirrhosis (LC) have impaired immunity and thus are predisposed to infections. Few studies have attempted to evaluate *Staphylococcus aureus* bacteremia (SAB) in LC patients. Therefore, this study prospectively evaluated the clinical characteristics and outcomes of 642 episodes of SAB from August 1, 2008 to September 31, 2010. Of 642 patients with SAB, 109 (17.0 %) were classified as LC patients whereas the remaining 533 (83.0 %) were classified as non-LC patients. The 30-day mortality rate of LC patients was significantly higher than that of patients with other diseases (32 % vs. 22 %, respectively; P=0.047). The 30-day mortality rates of patients with MSSA bacteremia and MRSA bacteremia were not significantly different among LC patients (35.1 % with MSSA vs. 26.9 % with MRSA; P=0.41). A univariate analysis of the 30-day mortality rate of LC patients with SAB for survivors and non-survivors showed that rapidly fatal or ultimately fatal according to the criteria of McCabe and Jackson (OR 5.0; 95 % CI 1.60–15.65), septic shock at initial presentation (OR 3.5; 95 % CI 1.18–10.39) and Child-Pugh class C (OR 2.8; 95 % CI 1.20–6.59) were associated with increased mortality. In contrast, the removal of the eradicable focus was associated with decreased mortality (OR 0.14; 95 % CI 0.04–0.52). Disease severity and liver dysfunction may be useful for predicting the prognosis of SAB in LC patients.

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Background

Cirrhosis of the liver is the terminal point of many multifactorial processes that lead to hepatic destruction and eventual death [1]. Patients with liver cirrhosis (LC) have impaired immunity and are predisposed to infections. A wide range of infections can decompensate hepatic status and drive LC patients toward death. *S. aureus* is accepted increasingly as an important pathogen in LC patients [2, 3]. Cirrhosis-specific scores such as the Model of End-Stage Liver Disease (MELD) and the Child-Pugh score (CP) have been reported to be good predictors of the short-term and long-term mortality of cirrhotic patients, even in patients with infections [4–6]. Consequently, the disease severity prediction for LC patients may need to be based on specific parameters that are different from those used for the general population [7]. Few studies have attempted to evaluate *S. aureus* bacteremia (SAB) in LC patients [8–10]. Therefore, the present study evaluated the clinical characteristics and outcomes of SAB in LC patients.

Materials and methods

Study design and population

A prospective SAB surveillance study has been performed since August 2008 at Asan Medical Center, which is a 2,700-bed tertiary affiliated hospital in Seoul, Republic of Korea. Daily active surveillance of blood cultures detected patients whose blood cultures were positive for *S. aureus*. This study included all SAB patients who were aged 16 years or older whereas it excluded patients who had already been enrolled within three months. Data from the surveillance study were collected prospectively from August 1, 2008 until September 31, 2010. A prospective cohort study was conducted to evaluate the clinical features and outcomes of SAB in LC patients. LC patients with any causes were identified during the SAB surveillance study and data on LC patients with SAB were collected.

The information collected from cases included baseline demographic information, underlying diseases, severity of diseases, LC etiology, degree of LC severity according to the CP class score and MELD score, underlying comorbid conditions, and the primary foci of bacteremia. Outcomes such as the 30-day mortality rate were assessed.

Definitions

SAB was defined by the isolation of *S. aureus* from at least one set of blood cultures obtained from patients with clinical signs of infection. Isolation of *S. aureus* from multiple cultures obtained from an individual patient was treated as a single episode of bacteremia. Based on the information found in medical records, isolates were classified as "community," "nosocomial," and "healthcare-associated" depending on where they were acquired [11]. Catheter-related infections (CRI) were considered the source of bacteremia if the catheter had been in place for at least 72 h and there was no other attributable source of bacteremia, and if one of the following criteria was met: (1) the culture of a specimen of purulent drainage from the insertion site grew *S. aureus* that had the same resistance pattern as the culture strain from the peripheral blood; (2) the semiquantitative culture of the removed catheter tip revealed ≥15 colony-forming units by the roll pate technique; (3) indicative differential time to positivity (i.e., the blood culture obtained through intravascular catheter became positive at least 2 h earlier than a positive simultaneous blood culture obtained from a peripheral vein) [12]. Persistent SAB was defined as the isolation of *S. aureus* in blood cultures obtained from peripheral veins or central lines on ≥7 consecutive days despite appropriate antibiotic administration for ≥5 days [13].

An LC diagnosis was established by histological criteria or based on clinical, analytical, and imaging findings. The primary focus of infection was based on evident clinical signs and/or symptoms [2]. The initial manifestation at the time of bacteremia was classified according to the International Sepsis Definitions, which include fever (body temperature>38.0°C), hypothermia (body temperature<36°C), tachycardia (heart rate>90 beats per min), tachypnea (respiratory rate>20 breaths per min), leukopenia (peripheral white blood cells counts<4000/mm^3), leukocytosis (peripheral white blood cells counts>12000/mm^3), and bandemia (bands>10 %). Sepsis was defined as specific inflammatory response syndrome (SIRS) in response to a confirmed infectious process, and severe sepsis was defined as sepsis with organ dysfunction, hypoperfusion, or hypotension. Septic shock was defined as sepsis-induced hypotension (systolic blood pressure<90 mm Hg or a drop in the mean arterial pressure>40 mm Hg from the baseline) that was nonresponsive to an intravenous fluid challenge, with signs of peripheral hypoperfusion [14].

The MELD score and CP score were used to compare the outcomes of LC patients with SAB according to the degree of LC severity. The MELD scores were computed using the online calculator available at http://www.mayoclinic.org/meld/mayomodel8.html. The high risk group was defined as a MELD score range of 21–40, or as a CP score class C. The mild to moderate risk group was defined as a MELD score range of 6–20, or as CP score classes A or B.

Blood culture, species identification, and susceptibility testing

Throughout the test period, all blood cultures were processed by the hospital microbiology laboratory using a standard blood culture system (BACTEC 730 or BACTEC 9240; Becton Dickinson, Franklin Lakes, NJ). Antibiotic susceptibilities were determined using a MicroScan (Dade Behring, West Sacramento, CA) or VITEK 2 (BioMérieux, Maray l'Etoile, France) system, according to the standard criteria described by the Clinical and Laboratory Standards Institute.

Statistical analysis

All results were analyzed using SPSS version 18.0 for Windows (SPSS Inc., Chicago, IL). The categorical variables were compared with Fisher's exact tests or Pearson χ^2 tests, whereas the continuous variables were compared using the Mann–Whitney *U*-test or the Student's *t*-test. All tests of significance were two-tailed and a *P*-value of<0.05 was considered to be statistically significant.

Results

Clinical characteristics of patients with SAB

From August 1, 2008 until September 31, 2010, a total of 726 episodes of SAB were recorded. Eighty-four patients were excluded because they were younger than 16 years, outpatients, or patients who had already been enrolled within three months. A total of 642 patients with SAB were used to evaluate the clinical features and outcomes of SAB. Of the 642 SAB patients, 109 (17.0 %) were classified as LC patients whereas the remaining 533 (83.0 %) were classified as non-LC patients.

Table 1 shows a comparison of the baseline clinical characteristics for the 642 patients with and without LC. LC patients were more frequently male (75.2 %) and solid organ transplant recipients (17.4 %), while they also had a higher incidence of alcoholism (22.0 %) and solid cancers (55.0 %), most of which were hepatocellular carcinomas (93.3 %, 56/60). Patients without LC had a greater incidence of hypertension (43.2 %), cardiovascular diseases (18.8 %) including myocardial infarction (MI) and chronic heart failure (CHF), and hematological malignancy (10.5 %). According to the McCabe and Jackson criteria, LC patients were more rapidly fatal or ultimately fatal (67.9 %). In terms of their underlying conditions, LC patients received more immunosuppressive therapy (18.3 %). However, the other underlying conditions at the time of SAB were not significantly different between LC patients and non-LC patients. As for primary focus of SAB, the most frequent sites of origin were CRI, although there was no difference of proportion on CRI between LC patients and non-LC patients (32.1 % vs. 33.2 %; P=0.91, respectively). In a subset of 212 patients with catheter related SAB, there was no significant difference in the 30-day mortality based on the presence or absence of LC (28.6 % vs. 20.0 %; P=0.26, respectively). The 30-day mortality rate (32.0 %) of LC patients was significantly higher than that of patients without LC (22.0 %).

Clinical characteristics of LC patients with SAB

Table 2 shows the clinical characteristics of LC patients with SAB. The most common cause of LC was hepatitis B virus (50.5 %). Alcohol (21.1 %) and hepatitis C virus (17.4 %) were the next most common causes. In terms of the CP classes, 50.5 % of cases were grade C and 32.1 % of cases were grade B. The median value for the CP class score was 9 (IQR, 7–11) and the median value of the MELD score was 14 (IQR, 10.0–20.5). Twenty-two patients (20.2 %) were in the ICU at the time of bacteremia. The primary foci of SAB were determined as the place of bacteremia acquisition. The most frequent sites of origin were catheter-related infection (32.1 %), unknown origin (20.2 %), skin and soft tissue infection (9.2 %), surgical site infection, and bone and joint infection (5.5 %).

In 57 patients (52.3 %), bacteremia was due to methicillin-susceptible *S. aureus* (MSSA), whereas it was attributable to methicillin-resistant *S. aureus* (MRSA) in 52 patients (47.7 %). Table 2 shows a comparison of the clinical characteristics with MRSA and MSSA. Patients with MRSA bacteremia experienced greater chronic renal insufficiency (9.6 %, P=0.02) and organ transplant operation (26.9 %, P=0.02). Other underlying diseases were not significantly different between MRSA and MSSA. The McCabe and Jackson criteria and APACHE II score were not significantly different. The LC etiology, proportion of CP class grades, and the median MELD scores were not significantly different. However, the median CP class score, 10 (IQR 7–12, P=0.04), was higher with MRSA than MSSA. In terms of the underlying conditions, recent surgery within 1 month, prior ICU care within 3 days, mechanical ventilation within 3 days, and indwelling catheter, including, central venous catheter, urinary catheter, and biliary drainage catheter, were significantly more common in patients with MRSA bacteremia than those with MSSA bacteremia. In terms of the SAB primary focus, catheter-related infection was significantly more common with MRSA bacteremia than MSSA bacteremia (50.0 % vs. 15.8 %, P<0.001). Pneumonia and surgical site infection were more common with MRSA bacteremia, although there was no significant difference. Bone and joint infections were significantly more common in patients with MSSA bacteremia than MRSA bacteremia (10.5 % vs. 0 %, P= 0.03). Skin and soft tissue infection, infective endocarditis, and urinary tract infection were more common in patients with MRSA bacteremia, although there was no significant difference. An eradicable focus was significantly more common in patients with MRSA bacteremia (59.6 %, P=0.01), although removal of the eradicable focus was not significantly different between the two groups. There was no significant difference between MRSA and MSSA in terms of persistent SAB (19.2 % vs. 7.0 %, P=0.08), the 10-day mortality (13.5 % vs. 14.0 %, P> 0.99), the 20-day mortality (23.1 % vs. 28.1 %, P=0.66), and the 30-day mortality rate (26.9 % vs. 35.1 %, P=0.41).

Factors associated with the 30-day mortality of LC patients with SAB

Table 3 shows the clinical characteristics and factors associated with the 30-day mortality rate of LC patients with SAB in terms of survivors and non-survivors. Non-survivors had more severe initial presentation than survivors. Rapidly fatal or ultimately fatal according to the criteria of McCabe and Jackson (88.2 % vs. 60.0 %; P=0.003),

Table 1 Clinical characteristics of liver cirrhosis (LC) patients with *S. aureus* bacteremia

Characteristic	Patients with LC (n=109) No. (%)	Patients without LC (n=533) No. (%)	P
Age, mean±SD	57±10.4	65±15.2	0.21
Male sex	82 (75.2)	338 (63.4)	0.02
Underlying disease[a]			
Solid cancer	60 (55.0)	201 (37.7)	0.001
Hematologic malignancy	3 (2.8)	56 (10.5)	0.01
Biliary disease	4 (3.7)	17 (3.2)	>0.999
Hypertension	17 (15.6)	230 (43.2)	<0.001
Diabetes mellitus	35 (32.1)	156 (29.3)	0.57
Alcoholism	24 (22.0)	16 (2.4)	<0.001
End-stage renal disease on dialysis	5 (4.6)	55 (10.3)	0.07
SOT	19 (17.4)	12 (2.3)	<0.001
HSCT (PBSCT, BMT)	1 (0.9)	9 (1.7)	0.71
COPD	2 (1.8)	23 (4.3)	0.29
Autoimmune disease	2 (1.8)	21 (3.9)	0.40
Cardiovascular disease (MI, HF)	5 (4.6)	100 (18.8)	<0.001
Severity of disease			
McCabe and Jackson criteria			<0.001
Non-fatal	35 (32.1)	308 (57.8)	
Rapidly fatal or ultimately fatal	74 (67.9)	221 (41.4)	
APACHE II score, median (IQR)	16 (12.0–21.0)	16 (12.0–22.0)	0.31
Septic shock at initial presentation	16 (14.7)	101 (18.9)	0.07
Underlying condition[a]			
Neutropenia (ANC<500, within 3 days)	3 (2.8)	34 (6.4)	0.18
Recent surgery (within 1 month)	19 (17.4)	122 (22.9)	0.21
Cancer chemotherapy (within 1 month)	18 (16.5)	76 (14.3)	0.72
Immunosuppressive therapy[b]	20 (18.3)	26 (4.9)	<0.001
Prior ICU care (within 3 days)	22 (20.2)	109 (20.5)	>0.999
Mechanical ventilation (within 3 days)	10 (9.2)	69 (12.9)	0.27
Central venous catheter (within 3 days)	42 (38.5)	248 (46.5)	0.27
Urinary catheter (within 3 days)	34 (31.2)	190 (35.6)	0.38
Biliary drainage catheter (within 3 days)	9 (8.3)	37 (6.9)	0.68
Primary focus of SAB			
Catheter-related infection (CVC)	35 (32.1)	177 (33.2)	0.91
Unknown origin	22 (20.2)	67 (12.6)	0.047
Skin & soft tissue infection	8 (7.3)	41 (7.7)	>0.999
Surgical site infection	6 (5.5)	40 (7.5)	0.55
Bone & joint infection	6 (5.5)	41 (7.7)	0.55
Pneumonia	3 (2.8)	47 (8.8)	0.047
Infective endocarditis	3 (2.8)	21 (3.9)	0.60
Urinary tract infection	1 (0.9)	10 (1.9)	0.70
30-day mortality	34 (32.0)	117 (22.0)	0.047

SOT solid organ transplant, *HSCT* hematopoietic stem cell transplantation, *PBSCT* peripheral blood stem cell transplant, *BMT* bone marrow transplant, *COPD* chronic obstructive pulmonary disease, *MI* myocardial infarction, *HF* heart failure, *IQR* interquartile range, *ANC* absolute neutrophil count, *ICU* intensive care unit, *SAB* *S. aureus* bacteremia, *SD* standard deviation

Data indicate numbers (%) of patients, unless otherwise indicated

[a] Some patients had>1 underlying disease or condition

[b] Receipt of steroid therapy for> 10 days or use of other immunosuppressant for>1 week within the previous month

septic shock at initial presentation (26.5 % vs. 9.3 %; P= 0.02), and infective endocarditis (8.8 % vs. 0 %; P=0.03) were significantly more common in non-survivors than survivors. The groups did not differ in the eradicable focus. However, the eradicable focus was removed significantly more from survivors than from non-survivors (42.7 % vs. 14.7 %; P=0.003). In terms of the high risk group of CP class C or MELD score (range 21–40), CP class C was significantly more common in non-survivors than survivors (67.6 % vs. 42.7 %; P=0.02), whereas the high risk MELD score (range 21–40) was not related to the 30-day mortality. In the univariate analysis of the 30-day mortality rate of LC

Table 2 Clinical characteristics of liver cirrhosis (LC) patients with *S. aureus* bacteremia

Characteristic	Total (*n*=109) No. (%)	MRSA (*n*=52) No. (%)	MSSA (*n*=57) No. (%)	*P*
Age, mean±SD	57.6±10.4	56.7±10.4	58.5±10.3	0.07
Male sex	87 (79.8)	41 (78.8)	46 (80.7)	0.82
Underlying disease[a]				
Solid cancer	60 (55.0)	28 (53.8)	32 (56.1)	0.85
Hematologic malignancy	4 (3.7)	2 (3.8)	2 (3.5)	>0.99
Biliary disease	5 (4.6)	4 (7.7)	1 (1.8)	0.19
Hypertension	17 (15.6)	11 (21.2)	6 (10.5)	0.19
Diabetes mellitus	35 (32.1)	19 (36.5)	16 (28.1)	0.41
Alcoholism	24 (22.0)	11 (21.2)	13 (22.8)	>0.99
Chronic renal failure without dialysis	5 (4.6)	5 (9.6)	0	0.02
End-stage renal disease on dialysis	5 (4.6)	4 (7.7)	1 (1.8)	0.19
SOT	19 (17.4)	14 (26.9)	5 (8.8)	0.02
HSCT (PBSCT, BMT)	1 (0.9)	1 (1.9)	0	0.48
COPD	2 (1.8)	0	2 (3.5)	0.50
Autoimmune disease	2 (1.8)	2 (3.8)	0	0.22
Cardiovascular disease (MI, HF)	4 (3.7)	2 (3.8)	2 (3.5)	>0.99
Severity of disease				
McCabe and Jackson criteria				0.92
Non-fatal	34 (31.2)	17 (32.7)	17 (29.8)	
Rapidly fatal or ultimately fatal	75 (68.8)	35 (67.3)	40 (70.2)	
APACHE II score, median (IQR)	16.0 (12.0–21.0)	17.0 (13.5–23.0)	15.0 (12.0–19.3)	0.14
Etiology of liver cirrhosis				0.52
Hepatitis B virus	55 (50.5)	27 (51.9)	28 (49.1)	
Hepatitis C virus	19 (17.4)	7 (13.5)	12 (21.1)	
Alcohol	23 (21.1)	10 (19.2)	13 22.8)	
Others	12 (11.0)	8 (15.4)	4 (7.0)	
Concomitant hepatocellular carcinoma	56 (51.4)	23 (44.2)	33 (57.9)	0.18
Child-Pugh class				0.62
Class A	19 (17.4)	8 (15.4)	11 (19.3)	
Class B	35 (32.1)	15 (28.8)	20 (35.1)	
Class C	55 (50.5)	29 (55.8)	26 (45.6)	
Child-Pugh class score, median (IQR)	9.0 (7.0–11.0)	10.0 (7.0–12.0)	9.0 (7.0–10.0)	0.04
MELD score, median (IQR)	14.0 (10.0–20.5)	13.5 (10.0–23.8)	14.0 (9.0–18.0)	0.67
Underlying condition[a]				
Neutropenia (ANC<500, within 3 days)	3 (2.8)	2 (3.8)	1 (1.8)	0.61
Recent surgery (within 1 month)	18 (16.5)	15 (28.8)	3 (5.3)	0.001
Cancer chemotherapy (within 1 month)	18 (16.5)	6 (11.5)	12 (21.1)	0.21
Immunosuppressive therapy[b]	25 (22.9)	15 (28.8)	10 (17.5)	0.18
Prior ICU care (within 3 days)	22 (20.2)	18 (34.6)	4 (7.0)	<0.001
Mechanical ventilation (within 3 days)	10 (9.2)	8 (15.4)	2 (3.5)	0.045
Central venous catheter (within 3 days)	42 (38.5)	32 (61.5)	10 (17.5)	<0.001
Urinary catheter (within 3 days)	34 (31.2)	27 (51.9)	7 (2.3)	<0.001
Biliary drainage catheter (within 3 days)	9 (8.3)	8 (15.4)	1 (1.8)	0.01
Primary focus of SAB				
Catheter-related infection (CVC)	35 (32.1)	26 (50.0)	9 (15.8)	<0.001
Unknown origin	22 (20.2)	8 (15.4)	14 (24.6)	0.34
Skin & soft tissue infection	10 (9.2)	2 (3.8)	8 (14.0)	0.10
Surgical site infection	6 (5.5)	4 (7.7)	2 (3.5)	0.42
Bone & joint infection	6 (5.5)	0	6 (10.5)	0.03

Table 2 (continued)

Characteristic	Total (n=109) No. (%)	MRSA (n=52) No. (%)	MSSA (n=57) No. (%)	P
Pneumonia	3 (2.8)	3 (5.8)	0	0.11
Infective endocarditis	3 (2.8)	0	3 (5.3)	0.25
Urinary tract infection	2 (1.8)	0	2 (3.5)	0.50
Metastatic infection	13 (11.9)	5 (9.6)	8 (14.0)	0.77
Eradicable focus	50 (45.9)	31 (59.6)	19 (33.3)	0.01
Removal of eradicable focus	37 (33.9)	25 (48.0)	12 (21.1)	0.38
Community-onset SAB	31 (28.4)	8 (15.4)	23 (40.4)	0.01
Persistent SAB	14 (12.8)	10 (19.2)	4 (7.0)	0.08
10-day mortality	15 (13.8)	7 (13.5)	8 (14.0)	>0.99
20-day mortality	28 (25.7)	12 (23.1)	16 (28.1)	0.66
30-day mortality	34 (31.2)	14 (26.9)	20 (35.1)	0.41

SOT solid organ transplant, *HSCT* hematopoietic stem cell transplantation, *PBSCT* peripheral blood stem cell transplant, *BMT* bone marrow transplant, *COPD* chronic obstructive pulmonary disease, *MI* myocardial infarction, *HF* heart failure, *IQR* interquartile range, *ANC* absolute neutrophil count, *ICU* intensive care unit, *SAB S. aureus* bacteremia, *SD* standard deviation, *MELD* Model of End-Stage Liver Disease, *MRSA* methicillin-resistant *S. aureus*, *MSSA* methicillin-susceptible *S. aureus*

Data are numbers (%) of patients, unless otherwise indicated

[a] Some patients had>1 underlying disease or condition

[b] Receipt of steroid therapy for>10 days or use of other immunosuppressant for>1 week within the previous month

patients with SAB for survivors and non-survivors, it was shown that rapidly fatal or ultimately fatal according to the criteria of McCabe and Jackson, septic shock at initial presentation, and CP class C were associated with increased mortality. In contrast, removal of the eradicable focus was associated with decreased mortality (OR 0.14; 95 % CI 0.04–0.52).

Discussion

The current study evaluated the epidemiology, clinical features, and outcomes of SAB in 109 LC patients. The main findings were as follows: (1) LC patients had distinct clinical features and more severe SAB at admission compared with patients with other diseases; (2) the mortality rate of LC patients was significantly higher than those of patients with other diseases; (3) the mortality rates with MRSA bacteremia and MSSA bacteremia were not significantly different in LC patients; (4) the severity of diseases and liver dysfunction were associated with increased mortality; (5) cirrhosis-specific scores such as the CP class were particularly useful for predicting the prognosis.

Cirrhosis of the liver is the terminal point of multifactorial processes that lead to hepatic destruction and eventual death [1]. It is well-known that cirrhotic patients are predisposed to infectious diseases and have a poor prognosis, and that a wide range of bacterial infections can decompensate hepatic status and lead to the death of such patients [1]. In the present study, LC patients were more often male (75.2 %) and solid organ transplant recipients (17.4 %), and they had a higher incidence of alcoholism (22.0 %) and solid cancers (55.0 %). Viral hepatitis (68 %) was the main cause of LC rather than alcohol use (21 %), which is consistent with a previous study of an Asian population [15]. They were more rapidly fatal or ultimately fatal (67.9 %) according to the McCabe and Jackson criteria. The mortality rate was higher in LC patients than patients with other diseases, as observed in other studies of high risk groups with LC [1, 2, 16, 17]. The 30-day mortality rate (32.0 %) of LC patients was significantly higher compared with patients with other diseases, which agrees with the results of previous studies [15, 16].

The etiologies of hospital-acquired infections have undergone changes and Gram-positive bacteria have emerged as the main causes of infections in hospitalized patients [18]. *S. aureus* is recognized as an important pathogen in cirrhotic patients [18]. In the present study, MSSA bacteremia accounted for 52.3 % of cases (57/109), while MRSA bacteremia accounted for 47.7 % (52/109). Previous studies assumed that patients with MRSA bacteremia had higher mortality and adverse outcomes than patients with MSSA bacteremia [19–21]. However, the 30-day mortality rate in the present study was not significantly different between MRSA bacteremia and MSSA bacteremia in LC patients (35.1 % with MSSA vs 26.9 % with MRSA, P=0.41). To strengthen the present study, we assessed additionally the 10-day mortality and the 20-day mortality. However, they were not also significantly different between two groups. This result is supported by a recent study of *S. aureus*

Table 3 Factors associated with 30-day mortality in patients with liver cirrhosis and SAB

Characteristic	Survivors	Non-survivors	Univariate analysis	
	(*n*=75)	(*n*=34)	*P*	OR (95 % CI)
Age, mean±SD	56.0±9.7	59.0±11.6	0.91	
Male sex	60 (80.0)	27 (79.4)	>0.99	
Solid cancer	38 (50.7)	22 (64.7)	0.21	
Hematologic malignancy	2 (2.7)	2 (5.9)	0.59	
Hypertension	11 (14.7)	6 (17.6)	0.78	
Diabetes mellitus	25 (33.3)	10 (29.4)	0.83	
Alcoholism	17 (22.7)	7 (20.6)	>0.99	
ESRD	3 (4.0)	2 (5.9)	>0.99	
COPD	1 (1.3)	1 (2.9)	>0.99	
Rapidly fatal or ultimately fatal	45 (60.0)	30 (88.2)	0.003	5.0 (1.60–15.65)
Septic shock at presentation	7 (9.3)	9 (26.5)	0.02	3.50 (1.18–10.39)
Recent surgery (within 1 month)	15 (20.0)	3 (8.8)	0.17	
Chemotherapy (within 1 month)	15 (20.0)	3 (8.8)	0.17	
Immunosuppressive therapy[b]	20 (26.7)	5 (14.7)	0.22	
Prior ICU care (within 3 days)	17 (22.7)	5 (14.7)	0.44	
Mechanical ventilation (within 3 days)	7 (9.3)	3 (8.8)	>0.99	
Primary focus of SAB				
Catheter related infection	25 (33.3)	10 (29.4)	0.83	
Unknown origin	14 (18.7)	8 (23.5)	0.61	
Skin & soft tissue infection	9 (12.0)	1 (2.9)	0.17	
Surgical site infection	2 (2.7)	4 (11.8)	0.37	
Bone & joint infection	2 (2.7)	4 (11.8)	0.08	
Pneumonia	2 (2.7)	1 (2.9)	>0.99	
Infective endocarditis	0	3 (8.8)	0.03	3.91×10^9
Eradicable focus	36 (48.0)	14 (41.2)	0.54	
Removal of eradicable focus	32 (42.7)	5 (14.7)	0.003	0.14 (0.04–0.52)
Child-Pugh class C	32 (42.7)	23 (67.6)	0.02	2.81 (1.20–6.59)
MELD score, high-risk class	16 (21.3)	11 (32.4)	0.24	

OR odds ratio, *CI* confidence interval, *ESRD* end stage renal disease, *COPD* chronic obstructive pulmonary disease, *ICU* intensive care unit, *MELD* Model of End-Stage Liver Disease

Data are numbers (%) of patients, unless otherwise indicated

infection in chronic liver disease, where the mortality rate of the MRSA group was not significantly different from that of the MSSA group in patients with liver disease [16]. This previous study suggested that methicillin resistance was not the main factor involved in poor prognosis in a population of patients with chronic liver diseases, whereas old age, underlying conditions, and concomitant bacteremia were independently associated with a higher mortality rate in patients [16]. In another previous study including 238 patients with SAB, the difference in mortality between MRSA and MSSA bacteremia in patients with eradicable foci was not significant [17]. In the present study, LC patients with MRSA bacteremia had more eradicable foci, and removed eradicable foci more than those with MSSA bacteremia.

The univariate analysis conducted in the present study showed that factors associated with mortality in LC patients with SAB were rapidly fatal or ultimately fatal according to the criteria of McCabe and Jackson, septic shock at initial presentation, and CP class C. Inversely, removal of the eradicable focus was associated with decreased mortality in LC patients with SAB. It was not possible to perform a multivariate logistic regression analysis because of the small number of patients who died. Bacteremia, CP score, and MELD score have been previously reported as risk factors for mortality in LC patients with infection [1, 5, 6, 22]. In the present study, patients with a high risk class MELD score were more likely to be non-survivors, although there was no significant difference. Patients with CP class C were significantly more likely to be non-survivors. In a recent study, the MELD score was

found to be a good predictor of death and ICU admission in patients with LC and community-acquired pneumonia (CAP) [7]. Therefore, the severity of liver dysfunction and removal of the eradicable focus in LC patients with SAB might be an important predictor of prognosis.

This study had several limitations. First, our study was performed with patients in a single, large tertiary care center and the results may be different from those in other hospitals. Second, this study had a limited number of patients and a relatively short duration. A longer period and a greater number of patients may make it possible to reach more concrete conclusions. Finally, this study was a non-blinded, prospective observational study. Therefore, unmeasured confounding factors and hidden bias might have affected our results. Despite these limitations, this study provides a greater understanding of SAB in LC patients, which may provide a basis for future studies.

Conclusion

In this study, the mortality rates of LC patients with SAB were significantly higher than those of patients with other diseases. The severity of diseases and liver dysfunction were also associated with increased mortality. In contrast, removal of the eradicable focus was associated with decreased mortality. Cirrhosis-specific scores such as the CP class and whether or not the eradicable focus was removed may be particularly useful for predicting the prognosis of SAB in LC patients.

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Conflict of interest The authors declare that they have no conflict of interest.

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