




# Association of methicillin resistance with mortality of hospital-acquired *Staphylococcus aureus* bacteremia

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## Abstract

**Objective:** Methicillin-resistant (MR) *Staphylococcus aureus* bacteremia (SAB) is associated with higher mortality rates than methicillin-susceptible (MS) SAB. This study assessed potential predictors of mortality and evaluated the association of methicillin resistance with mortality in patients with SAB.

**Methods:** We conducted a retrospective cohort study in patients with hospital-acquired SAB, from 2009 to 2018. Clinical features of patients with MR-SAB were compared with those of patients with MS-SAB and predictors of 30-day mortality were determined using Cox regression analysis.

**Results:** Among 162 patients, 56.8% had MR-SAB. Overall 30-day mortality was 19.1%; MR-SAB had higher mortality (25.0%) than MS-SAB (11.4%). Univariate analysis highlighted long-term hospitalization, prior antibiotics use, and delayed initiation of appropriate antibiotics as risk factors. Cox regression analysis showed that respiratory tract source, Pitt bacteremia score, Charlson comorbidity index, and appropriate antibiotic therapy within 24 hours were independently and significantly associated with 30-day mortality outcome.

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**Conclusions:** Methicillin resistance was not an independent risk factor for mortality in patients with SAB. Early, appropriate antibiotic treatment is an important prognostic factor.

### Keywords

Appropriate antibiotics, bacteremia, methicillin resistance, mortality, *Staphylococcus aureus*, Methicillin-resistant *Staphylococcus aureus*

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## Introduction

Bacteremia, one of the most serious hospital-acquired infections, prolongs the length of hospital stay, increases the cost of healthcare, and has a high fatality rate. Bacteremia caused by *Staphylococcus aureus*, the second most common cause of bacteremia after coagulase-negative staphylococci, has a crude mortality rate of 20% to 40%, indicating a poor prognosis.<sup>1–5</sup> According to differences in antimicrobial susceptibility, *S. aureus* is classified into methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA). In Japan, the proportion of MRSA and MSSA in blood culture isolates is approximately 50%, and the mortality rate of bacteremia owing to MRSA is 1.5- to 2-fold higher than that of bacteremia caused by MSSA.<sup>2,6–8</sup>

Although numerous studies have been conducted to investigate the association of methicillin resistance with mortality rates in patients with *S. aureus* bacteremia (SAB), conflicting results have been reported.<sup>2,6,9</sup> Increased mortality associated with MRSA bacteremia may be partially owing to delays caused by inappropriate antibiotic selection, which can occur when causative species and antibiotic susceptibilities are not known. Whereas several studies have shown that appropriate empirical antimicrobial therapy can have a positive impact

on patient outcomes,<sup>10–12</sup> other publications have indicated that appropriate empirical therapy does not significantly affect patient outcomes.<sup>13–15</sup> Therefore, it is unclear whether the increase in mortality associated with MRSA bacteremia is owing to a delay in administering appropriate antimicrobial therapy, differences in strain virulence, or other pathogen–host factors.

Accordingly, in this study, our aim was to determine the clinical features of patients with MRSA bacteremia to identify the predictors of mortality and to evaluate the association of methicillin resistance with mortality in patients with SAB.

### Ethical considerations

This study was approved by the institutional review board of the Faculty of Medical Sciences, University of Fukui (approval number: 20120089). The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The requirement for informed consent was waived owing to the retrospective nature of the study.

### Study design and population

This retrospective cohort study was conducted at the University of Fukui Hospital, a 600-bed secondary and tertiary care center in Japan. All hospitalized

patients at least 16 years of age whose blood cultures tested positive for *S. aureus* between January 2009 and December 2018 were included, provided the infection occurred more than 48 hours after hospital admission. Only the first episode for each patient was included in the analysis. Patients with polymicrobial bloodstream infection and those diagnosed with microbial contamination were excluded.

### Data collection

The following data were collected from medical charts to evaluate the severity of illness at onset of SAB: age; sex; body weight; serum albumin level; underlying diseases; intensive care unit stay; neutrophil count; presence of a central venous catheter (CVC); use of immunosuppressants, corticosteroids, anticancer chemotherapy, or antimicrobial agents (within 30 days prior to SAB); source of bacteremia; length of hospital stay before SAB onset; survival at 14, 30, and 90 days after SAB onset; time to administration of appropriate antibiotics; time to blood culture positivity (TTP);<sup>16</sup> Pitt bacteremia score (PBS);<sup>17</sup> and Charlson comorbidity index (CCI).<sup>18</sup>

### Definitions

SAB was defined as the presence of at least one *S. aureus*-positive blood culture in patients with signs and symptoms consistent with an infection.<sup>19</sup> The onset of SAB was defined as the date of sampling for the first *S. aureus*-positive blood culture. The source of bacteremia was determined using criteria set by the Centers for Disease Control.<sup>20</sup> Primary bacteremia indicates the condition when the source of bacteremia cannot be identified. Antimicrobial therapy was considered appropriate if the antimicrobial agent had *in vitro* activity against the isolated *S. aureus* strain. Vancomycin, teicoplanin, arbekacin,

linezolid, and daptomycin are suggested as appropriate antibiotics for MRSA treatment. The time to initiation of appropriate antibiotics was defined as the interval between SAB onset and initiation of appropriate antibiotics.

### Statistical analysis

All-cause 30-day mortality was used as a prognostic index. Statistical analysis was performed using the  $\chi^2$  test or Fisher's exact test for categorical variables and the Student *t*-test or Mann-Whitney U test for continuous variables. Multivariate Cox regression analysis was used to control the effects of confounding variables so as to identify variables independently associated with 30-day mortality. Variables with *P* values <0.1 in the univariate analysis were included in the multivariate analysis. Hazard ratios (HRs) and their 95% confidence intervals (CIs) were calculated. All *P* values were two-tailed, and results with *P* values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 17.0 (SPSS Japan Inc., Tokyo, Japan).

## Results

### Patient characteristics

In total, 315 patients with SAB were identified during the study period. Of the total patients, 162 fulfilled the inclusion criteria and were enrolled. We excluded 153 patients; 123 patients developed SAB within 48 hours after hospital admission, 9 were less than 16 years of age, 6 had polymicrobial infection, and 15 patients were diagnosed with microbial contamination. The mean patient age was 69.1 years, and 42.0% of patients were women. The overall 14-, 30-, and 90-day mortality rates were 10.5%, 19.1%, and 27.8%, respectively.

### Comparison of clinical features in patients with MRSA and MSSA bacteremia

Of the 162 included patients, 70 (43.2%) had MSSA bacteremia and 92 (56.8%)

had MRSA bacteremia. The population characteristics for both groups are specified in Table 1. Significant differences in clinical characteristics between the MSSA and MRSA groups were found for several

**Table 1.** Comparison of clinical features in patients with MSSA and MRSA bacteremia.

Characteristic	MSSA (N = 70)	MRSA (N = 92)	P
Age (years), mean $\pm$ SD	67.6 $\pm$ 13.9	70.3 $\pm$ 14.5	0.128
Female sex	31 (44.3)	37 (40.2)	0.603
Body weight (kg), mean $\pm$ SD	55.5 $\pm$ 13.4	55.1 $\pm$ 10.5	0.601
Serum albumin (g/dL), mean $\pm$ SD	2.9 $\pm$ 0.6	2.7 $\pm$ 0.6	0.099
Underlying disease			
Malignancy	34 (48.6)	40 (43.6)	0.519
Chronic heart disease	23 (32.9)	34 (37.2)	0.588
Diabetes mellitus	20 (28.6)	31 (33.0)	0.487
Chronic renal failure	14 (20.0)	16 (17.0)	0.688
Liver cirrhosis	8 (11.4)	7 (8.5)	0.406
Respiratory disease	6 (8.6)	13 (13.8)	0.276
Intensive care unit stay (days)	6 (8.6)	11 (12.0)	0.645
Neutropenia (<500/ $\mu$ L)	3 (4.3)	7 (7.4)	0.517
Presence of CVC	35 (50.0)	60 (64.9)	0.064
Immunosuppressants	2 (2.9)	2 (2.1)	1.000
Corticosteroids	9 (12.9)	8 (8.5)	0.392
Anticancer chemotherapy	21 (30.0)	19 (20.2)	0.172
Antimicrobial agents	17 (24.3)	66 (72.3)	<0.001
Source of bacteremia			
Primary	23 (32.9)	30 (31.9)	0.973
Catheter-related	35 (50.0)	41 (44.7)	0.492
Skin/soft tissue	6 (8.6)	9 (9.6)	0.792
Respiratory tract	3 (4.3)	2 (3.2)	0.653
Urinary tract	2 (2.9)	3 (3.2)	1.000
Other	1 (1.4)	7 (7.6)	0.139
Length of stay before bacteremia onset (days), mean $\pm$ SD	19.9 $\pm$ 21.4	48.5 $\pm$ 43.6	<0.001
Mortality			
14-day	2 (2.9)	15 (16.3)	0.006
30-day	8 (11.4)	23 (25.0)	0.030
90-day	13 (18.6)	32 (34.8)	0.022
Initiation of appropriate antibiotic therapy			
$\leq$ 24 hours	69 (98.6)	52 (56.5)	<0.001
$\leq$ 48 hours	70 (100)	67 (72.8)	<0.001
TTP (hours), mean $\pm$ SD	15.1 $\pm$ 13.3	17.6 $\pm$ 14.4	0.280
PBS, mean $\pm$ SD	1.7 $\pm$ 1.4	2.3 $\pm$ 1.8	0.038
CCI, mean $\pm$ SD	2.9 $\pm$ 2.0	2.8 $\pm$ 1.8	0.755

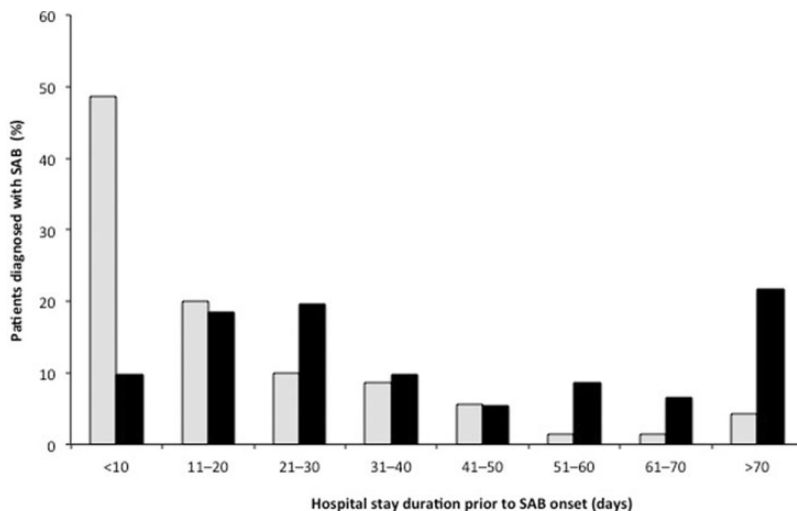
Data are n (%), unless otherwise indicated.

MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; SD, standard deviation; CVC, central venous catheter; TTP, time to blood culture positivity; PBS, Pitt bacteremia score; CCI, Charlson comorbidity index.

variables. The proportion with prior use of antimicrobial agents in the MRSA group was significantly higher than that in the MSSA group ( $P < 0.001$ ). As shown in Figure 1, the length of hospital stay before onset of bacteremia was significantly longer in the MRSA group than that in the MSSA group ( $P < 0.01$ ). The PBS for the MRSA group was significantly higher than that for the MSSA group ( $P = 0.038$ ). The 14-, 30-, and 90-day mortality rates of patients with MRSA bacteremia were higher than those of patients with MSSA bacteremia (2.9% vs. 16.3%,  $P = 0.006$ ; 11.4% vs. 25.0%,  $P = 0.030$ ; 18.6% vs. 34.8%,  $P = 0.022$ , respectively). Moreover, initiation of appropriate antibiotic therapy was significantly delayed in the MRSA group at 24 and 48 hours after onset (98.6% vs. 56.5%; 100% vs. 72.8%, respectively; both  $P < 0.001$ ).

### Risk factors associated with 30-day mortality

Table 2 shows the results of univariate analysis of risk factors for 30-day mortality of SAB in patients who died and those who survived. The proportion of patients with MRSA bacteremia ( $P = 0.030$ ) and respiratory tract source ( $P < 0.001$ ) among patients who died (“non-surviving” group) were significantly higher than those in who survived (“surviving” group). Patients who died had higher PBS ( $P = 0.018$ ) and CCI ( $P = 0.002$ ) values than surviving patients. The number of patients in the surviving group who received appropriate antibiotics within 24 hours was higher than that in the non-surviving group (78.6% vs. 58.1%;  $P = 0.018$ ). However, in the surviving and non-surviving groups, there were no significant differences between the number of



**Figure 1.** Duration of hospital stay versus bacteremia onset. Distribution of patients with MSSA (gray bars) and MRSA (black bars) bacteremia according to length of hospital stay (number of days post-admittance) at the time of bacteremia onset. The duration of pre-SAB hospital stay in patients with MRSA bacteremia was significantly longer than for those with MSSA bacteremia (mean  $\pm$  standard deviation  $19.9 \pm 21.4$  vs.  $48.5 \pm 43.6$ ; median [interquartile range] 12 [6–27] vs. 33 [17–65];  $P < 0.001$ ).

MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; SAB, *S. aureus* bacteremia.

**Table 2.** Univariate analysis of risk factors for 30-day mortality in *Staphylococcus aureus* bacteremia.

Characteristic	Survival (N = 131)	Death (N = 31)	P
Age (years), mean $\pm$ SD	67.9 $\pm$ 13.9	72.2 $\pm$ 13.2	0.056
Female sex	56 (42.7)	12 (38.7)	0.682
Body weight (kg), mean $\pm$ SD	56.1 $\pm$ 11.9	54.0 $\pm$ 11.0	0.491
Serum albumin (g/dL), mean $\pm$ SD	2.8 $\pm$ 0.6	2.7 $\pm$ 0.6	0.307
MRSA	69 (52.7)	23 (74.2)	0.030
Underlying disease			
Malignancy	57 (43.5)	17 (54.8)	0.317
Heart disease	41 (31.3)	9 (29.0)	0.977
Diabetes mellitus	44 (33.6)	7 (22.6)	0.235
Chronic renal failure	22 (16.8)	8 (25.8)	0.303
Liver cirrhosis	10 (7.6)	5 (16.1)	0.167
Respiratory disease	13 (9.9)	6 (19.4)	0.209
Intensive care unit stay (days)	14 (10.7)	3 (9.7)	0.869
Neutropenia (<500/ $\mu$ L)	9 (6.9)	1 (3.2)	0.448
Presence of CVC	77 (58.8)	18 (58.1)	0.902
Immunosuppressants	4 (3.1)	0	0.325
Corticosteroids	14 (10.7)	3 (9.7)	0.869
Anticancer chemotherapy	31 (23.7)	9 (29.0)	0.643
Antimicrobial agents	67 (51.1)	16 (51.6)	0.963
Source of bacteremia			
Primary	36 (27.5)	13 (41.9)	0.115
Catheter-related	66 (50.4)	10 (32.3)	0.069
Skin/soft tissue	14 (10.7)	1 (3.2)	0.197
Respiratory tract	1 (0.8)	4 (12.9)	<0.001
Urinary tract	5 (3.8)	0	0.269
Other	9 (6.9)	3 (9.7)	0.701
Length of stay before bacteremia onset (days)	31.4 $\pm$ 29.8	48.2 $\pm$ 42.0	0.072
Initiation of appropriate antibiotics			
$\leq$ 24 hours	103 (78.6)	18 (58.1)	0.018
$\leq$ 48 hours	112 (85.5)	24 (77.4)	0.271
TTP (hours), mean $\pm$ SD	17.5 $\pm$ 15.4	13.6 $\pm$ 6.2	0.239
PBS, mean $\pm$ SD	1.8 $\pm$ 1.4	2.9 $\pm$ 2.4	0.018
CCI, mean $\pm$ SD	2.75 $\pm$ 1.87	3.86 $\pm$ 2.0	0.002

Data are n (%), unless otherwise indicated.

MRSA, methicillin-resistant *S. aureus*; SD, standard deviation; CVC, central venous catheter; TTP, time to blood culture positivity; PBS, Pitt bacteremia score; CCI, Charlson comorbidity index.

patients who had received appropriate antibiotics within 48 hours (85.5% vs. 77.4%).

Multivariate analysis showed that respiratory tract source (HR, 5.26; 95% CI, 1.75–15.79;  $P=0.003$ ), initiation of appropriate antibiotics within 24 hours (HR, 0.35; 95% CI, 0.16–0.74;  $P=0.006$ ), PBS

(HR, 1.22; 95% CI, 1.03–1.45,  $P=0.019$ ), and CCI (HR, 1.32; 95% CI, 1.09–1.60,  $P=0.004$ ) were independent factors associated with 30-day mortality outcome (Table 3). HRs for CCI and PBS are given for 1-point increments in the index and score, respectively. MRSA, however, was

**Table 3.** Multivariate analysis related to 30-day mortality.

Variable	Adjusted HR (95% CI)	P
Age	1.02 <sup>a</sup> (0.98–1.05)	0.322
MRSA	1.67 (0.63–4.38)	0.301
Source of bacteremia		
Catheter-related	0.58 (0.27–1.28)	0.179
Respiratory tract	5.26 (1.75–15.79)	0.003
Initiation of appropriate antibiotics ( $\leq 24$ hours)	0.35 (0.16–0.74)	0.006
PBS	1.22 <sup>b</sup> (1.03–1.45)	0.019
CCI	1.32 <sup>b</sup> (1.09–1.60)	0.004

HR, hazard ratio; CI, confidence interval; MRSA, methicillin-resistant *S. aureus*; PBS, Pitt bacteremia score; CCI, Charlson comorbidity index.

<sup>a</sup>Per 1-year increment. <sup>b</sup>Per 1-point increment.

not identified as an independent risk factor for 30-day mortality after adjusting for other variables.

## Discussion

In this study, we observed significant differences in clinical outcomes between patients with MRSA and MSSA bacteremia. Consistent with the results of previous studies,<sup>2,6–8</sup> the mortality rates of patients with MRSA bacteremia were 2- to 5-fold higher than those of patients with MSSA bacteremia. In the current study, respiratory tract source, PBS, and CCI were identified as independent risk factors for 30-day mortality. Furthermore, early appropriate antibiotic therapy (<24 hours) was identified as an independent factor for an improved prognosis of SAB. This is in accordance with recommended SAB management strategies and current knowledge that timely administration of appropriate antibiotics may improve outcomes in some patients.<sup>21,22</sup>

Univariate analysis of risk factors for 30-day mortality of SAB in surviving patients and in those who died showed that the proportion of patients with MRSA bacteremia was significantly higher in the non-surviving group. However, in

multivariate analysis, MRSA bacteremia was not identified as an independent risk factor for 30-day mortality of SAB. This observation is not entirely surprising when considering current data on MRSA and mortality. The association of antibacterial resistance with mortality is complex and remains poorly understood. This association is likely influenced by various host factors and host–pathogen interactions. Whether the observed increased mortality is attributable to pathogen-specific factors, such as increased virulence, poor response to antibiotic therapy, or both, requires further study.<sup>21,23</sup>

We compared the clinical characteristics of patients with MSSA and MRSA bacteremia. Current knowledge on the impact of patient factors on SAB outcome is limited, with the only consistent predictors of SAB outcome being the presence of comorbidities and patient age<sup>21</sup>. In the current study, there was no significant difference in age between the MSSA and MRSA groups; however, the cohort mostly included older patients (age  $69.1 \pm 14.3$  years) and was not representative of a broad age range. No significant difference in the severity of comorbidities, as measured by the CCI, was observed between patients with MRSA and those with MSSA. Although the severity of



acute illness (as measured by the PBS) was significantly greater in patients with MRSA, the mean PBS score of this group (as with that of the MSSA group) was less than 4, and the proportion of patients with a PBS of more than 4 was not significantly different between the two groups (7.1% MSSA vs. 12.0% MRSA,  $P=0.452$ ). A score greater than 4 is routinely considered indicative of critical illness or increased risk of death. Univariate analysis of risk factors for 30-day mortality of SAB in surviving patients and in those who died showed that PBS and CCI were both significantly greater in non-surviving patients. Liao et al.<sup>24</sup> reported that the mean PBS for the non-surviving group of 59 patients with SAB was 5.9; among those patients, 24 died within 3 days of hospitalization. In the current study, the mean PBS for the non-surviving group was 2.3; that is, the severity of bacteremia was relatively low in many patients. Previous conflicting findings regarding the comparison of mortality rates in patients with MRSA and MSSA bacteremia may be explained by differences in patient condition, patient background, or suboptimal response to vancomycin compared with beta-lactams.<sup>25,26</sup> Furthermore, methodological differences related to study design, definitions, and analyses should be considered when comparing different studies. Another potential factor for poorer prognosis of MRSA bacteremia and conflicting data is the possibility that MRSA strains are more virulent. Although results from various clinical studies support this notion, *in vitro* investigations have yielded contradictory results.<sup>23</sup> The most likely cause of these conflicting data is heterogeneity of the bacterial population, with MSSA populations containing resistance cells, which are then selected for on treatment with non-MRSA-targeting antibiotics; this may influence the subsequent clinical response.<sup>23</sup>

In our study, we found that the number of patients with low serum albumin levels and the presence of CVC was higher in the MRSA group than in the MSSA group, suggesting that more patients in the MRSA group were malnourished; this is consistent with findings that malnutrition is associated with poor clinical outcomes among hospitalized patients.<sup>27</sup> Furthermore, the number of patients with prior use of antibiotics (within 30 days before SAB) and longer hospitalization was higher in the MRSA group than in the MSSA group. These data are in accordance with previous studies showing that these are considered risk factors for inducing drug-resistant bacterial infections, such as MRSA bacteremia.<sup>2,28-34</sup>

Current SAB management strategies emphasize the value of timely initiation of appropriate antibiotic therapy<sup>21</sup>. In the current study, we found that initiation of appropriate antibiotic therapy was delayed in most patients with MRSA bacteremia. Only 52 (56.5%) of 92 patients were administered appropriate antibiotics within 24 hours in the MRSA group, compared with 69 (98.6%) of 70 patients in the MSSA group. This could be because beta-lactam antibiotics, which are routinely used as first-line therapy in SAB, exhibit antibacterial activity against MSSA but not MRSA. Therefore, anti-MRSA antibiotics were only administered after obtaining *in vitro* culture results, causing a delay in the initiation of appropriate antibiotic therapy. Furthermore, we found that the initiation of appropriate antibiotic therapy within 24 hours improved patient outcomes. This is in accordance with previous studies in which timely administration (within 48 hours) of empiric antibiotics was associated with decreased mortality and was positively associated with improved clinical outcomes.<sup>10,11,21</sup> Nevertheless, the benefits and importance of early appropriate empirical antibiotic treatments of MRSA are



contradicted by many studies showing no benefit with early administration of appropriate empirical antibiotics for MRSA treatment.<sup>13–15</sup> These contrasting results could be attributed to differences in the definition of appropriate antibiotic therapy and patient backgrounds. In previous studies, initiation of appropriate antimicrobial treatment varied from 24 to 72 hours after blood culture collection.<sup>4,11,13,14</sup> In other studies, the time to initiation of appropriate antibiotic treatment was defined either as the time since a positive blood culture was reported or the time after bacteremia had developed.<sup>12,15</sup> In the current study, multivariate analysis was performed using appropriate antibiotic treatment within 24 hours of blood culture collection as a variable, based on the results of univariate analysis. Furthermore, some previous studies were conducted without distinguishing between community onset and hospital onset; moreover, whether SAB was owing to community onset may not be known. Because this study was limited to in-hospital onset, the time from bacteremia onset to the initiation of appropriate antimicrobial treatment could be accurately evaluated. Furthermore, the poorer prognosis of MRSA bacteremia compared with MSSA bacteremia could be owing to the inefficacy of vancomycin in addition to the delay in appropriate antibiotic treatment. Several studies have suggested that vancomycin is less effective than beta-lactam antibiotics against *S. aureus*.<sup>25,26</sup> Although early initiation of appropriate antibiotics may improve prognosis, further research is still required to clarify the relationship between the timing of antimicrobial initiation and prognosis.

The current study highlighted the importance of initiating early therapy using anti-MRSA agents in patients with MRSA bacteremia. It is necessary to carefully evaluate the risk of MRSA infection at the onset of bacteremia, taking advantage of early

diagnosis tools such as detection of the *mecA* gene, and initiating anti-MRSA antibiotic therapy if the risk of MRSA infection is high. Identifying patient factors that can be used as indicators of MRSA bacteremia could be valuable in ensuring timely identification and treatment of patients with MRSA.

This study had some limitations. First, the data were collected retrospectively and therefore could have been misinterpreted. Moreover, other unknown confounders may have been omitted. Second, this was a single-center study with a small number of patients and limited information. Third, in our cohort, the proportion of patients with MRSA bacteremia exceeded 50% versus those with MSSA bacteremia. Furthermore, most patients were older, with mean ( $\pm$  SD) age 69.1 ( $\pm$  14.3) years; thus, the data may not be generalizable to other age groups. Furthermore, because the most frequently administered anti-MRSA drug was vancomycin, we could not evaluate differences in efficacy between vancomycin and other anti-MRSA drugs.

In conclusion, methicillin resistance was not a significant predictor of mortality in patients with SAB in a hospital setting with a high prevalence of MRSA. Respiratory tract source, PBS, and CCI were identified as risk factors associated with mortality in patients with SAB, and early appropriate antibiotic therapy (<24 hours) was identified as an independent factor to improve SAB prognosis. Furthermore, prior antibiotic exposure, long-term hospitalization, and a high PBS could serve as indicators of an increased risk of MRSA in patients with suspected SAB.

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### Author contributions

T. Aratani, H. Tsukamoto, and N. Goto conceptualized and designed the study. T. Aratani, H. Tsukamoto, T. Higashi, T. Kodawara, and Y. Hida acquired the data. T. Aratani, H. Tsukamoto, N. Goto, R. Yano, and H. Iwasaki analyzed and interpreted the data. T. Aratani, H. Tsukamoto, and N. Goto drafted and critically revised the manuscript. All authors approved the final version of the manuscript.

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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